This is a digital copy of a book that was preserved for generations on library shelves before it was carefully scanned by Google as part of a project to make the world's books discoverable online.

It has survived long enough for the copyright to expire and the book to enter the public domain. A public domain book is one that was never subject to copyright or whose legal copyright term has expired. Whether a book is in the public domain may vary country to country. Public domain books are our gateways to the past, representing a wealth of history, culture and knowledge that's often difficult to discover.

Marks, notations and other marginalia present in the original volume will appear in this file - a reminder of this book's long journey from the publisher to a library and finally to you.

Usage guidelines

Google is proud to partner with libraries to digitize public domain materials and make them widely accessible. Public domain books belong to the public and we are merely their custodians. Nevertheless, this work is expensive, so in order to keep providing this resource, we have taken steps to prevent abuse by commercial parties, including placing technical restrictions on automated querying.

We also ask that you:

+ *Make non-commercial use of the files* We designed Google Book Search for use by individuals, and we request that you use these files for personal, non-commercial purposes.

+ *Refrain from automated querying* Do not send automated queries of any sort to Google's system: If you are conducting research on machine translation, optical character recognition or other areas where access to a large amount of text is helpful, please contact us. We encourage the use of public domain materials for these purposes and may be able to help.

+ *Maintain attribution* The Google "watermark" you see on each file is essential for informing people about this project and helping them find additional materials through Google Book Search. Please do not remove it.

+ *Keep it legal* Whatever your use, remember that you are responsible for ensuring that what you are doing is legal. Do not assume that just because we believe a book is in the public domain for users in the United States, that the work is also in the public domain for users in other countries. Whether a book is still in copyright varies from country to country, and we can't offer guidance on whether any specific use of any specific book is allowed. Please do not assume that a book's appearance in Google Book Search means it can be used in any manner anywhere in the world. Copyright infringement liability can be quite severe.

About Google Book Search

Google's mission is to organize the world's information and to make it universally accessible and useful. Google Book Search helps readers discover the world's books while helping authors and publishers reach new audiences. You can search through the full text of this book on the web at `http://books.google.com/`

LANE MEDICAL LIBRARY STANFORD
L656 .B81 1920 STOR
Exophthalmic goiter and its nonsurgical
24503424038

LANE
MEDICAL LIBRARY
SEAL OF THE LELAND STANFORD JUNIOR UNIVERSITY
1885
LEVI COOPER LANE FUND

LANE

MEDICAL LIBRARY

SEAL OF THE LELAND STANFORD JUNIOR UNIVERSITY

1885

LEVI COOPER LANE FUND

EXOPHTHALMIC GOITER
AND ITS
NONSURGICAL TREATMENT

EXOPHTHALMIC GOITER
AND ITS
NONSURGICAL TREATMENT

BY

ISRAEL BRAM, M.D.

INSTRUCTOR IN CLINICAL MEDICINE, JEFFERSON MEDICAL COLLEGE, PHILADELPHIA,
PA.; PHYSICIAN ON VISITING STAFF OF PHILADELPHIA GENERAL HOSPITAL;
MEMBER OF THE SOCIETY FOR STUDY OF INTERNAL SECRETIONS, ETC.

LIBRARY

ST. LOUIS
C. V. MOSBY COMPANY
1920

COPYRIGHT, 1920, BY C. V. MOSBY COMPANY
(All Rights Reserved)

Press of
C. V. Mosby Company
St. Louis

L656
B81
1920

TO

MY WIFE

In Grateful Appreciation of Her Untiring Devotion
This Work Is Affectionately Dedicated.

51142

PREFACE

In explaining the existence of this book, the title requires a word or two of comment. "Exophthalmic Goiter and Its Nonsurgical Treatment" partakes both of the usual and the unusual. Many books have been written on exophthalmic goiter,—some mediocre, others very valuable. These deal especially with amplified etiologic theories, minute technic of eliciting signs and symptoms, an elaborate description of pathologic specimens, and the relative merits of one *surgical* procedure over another. But little if any thought or space is given to remedial measures which do *not* require the knife. This is the *usual* book on the subject embraced by the first half of our title.

The *unusual* part of our title, that dealing with *nonsurgical* treatment, is the real excuse for the existence of this work. The author hastens to remark that his twelve years' study of diseases of the thyroid gland (many convictions and experiences of which are herein embodied) has led him to believe that the book will not only be tolerated, but will be found a help to the general practitioner of medicine.

This volume is not intended to serve the purpose of a comprehensive work on the advances made in thyroid experimentation, nor does the author intend to launch forth any new views concerning the mechanism of the chain of ductless glands of which the thyroid plays a leading rôle. No one can presume to place at the disposal of the reader the most important results of labors in endocrinology in one small treatise. The important facts—those bearing a practical relationship to Graves' disease, as well as the salient points concerned in the successful therapeutics of this disease, are particularly stressed upon. It is in this practical respect that the author hopes to serve the general practitioner in his efforts to overcome the ravages of a disease for many years considered refractory to treatment.

In offering the forthcoming views and facts to the reader, the author hopes (1) to stimulate a keener interest in the disease in question than has heretofore been evinced by the busy practitioner; (2) to convince him that exophthalmic goiter does not belong in the realm of surgery; (3) to persuade him eagerly to attempt an early diagnosis and institute the proper *nonsurgical* treatment with a will to win.

Numerous authorities have been consulted in the preparation of these pages. I am especially indebted to the editors of "Endocrinology," to McCarrison, Crotti, Roussy, Kocher and others, from whose valuable works many quotations have been excerpted, for which due credit is given. The bibliography mentions most of the other authors whose writings have been consulted for suggestions, and comments were made thereon. If, through stress of duties, the author has failed to give due credit to men whose material has been directly or indirectly consulted, he herewith extends his acknowledgment and grateful appreciation of the same. A few chapters, slightly modified, were in the form of the author's papers published in leading medical journals, especially the "New York Medical Journal," "Archives of Diagnosis," "International Clinics," "Endocrinology," and "American Medicine," the utilization of which was kindly permitted by the respective editors.

It is with extreme pride and pleasure that I acknowledge the spiritual and material encouragement of Prof. Solomon Solis-Cohen, of the Jefferson Medical College, in whose service as assistant I am fortunate enough to be. The wide endeavors of this famous internist as pioneer in many branches of medicine, his keen interest in endocrinology, and above all, his admirable personality, are qualities which encourage, enthuse and spur on in emulation the younger men who happily find themselves within the sphere of his activities.

To my friend, Dr. Aaron Barlow, I acknowledge my grateful appreciation for assistance in the reading and correction of the proofs.

Finally, I am especially indebted to my wife through whose untiring energy and incessant encouragement this small work was made possible. Not only was she an invaluable aid in the preparation of the subject-matter and in the translation of works of foreign authors, but also with regard to the lucidity of views and continuity of expression, attributes which are highly essential in the discussion of matters pertaining to endocrinology. I may also say that to her is due the credit for assistance in the preparation of the index, a supplement of inestimable value in all works of a scientific nature.

I. Bram.

Philadelphia, Pa.

CONTENTS

Page

INTRODUCTION 17

CHAPTER I

ANATOMY 25

Shape and Relations, 25; Structure, 27; Histology, 27; Blood Supply, 28; Lymphatics, 29; Nerve Supply, 29; Accessory Thyroids, 30; Remarks, 30; Parathyroid Glands, 33; Development, 34.

CHAPTER II

PHYSIOLOGY OF THE THYROID 36

Structure, 36; Factors Governing Secretion, 38; Thyroid Secretion, 39; Iodine Content, 41; Iodothyrin, 42; Iodothyroglobulin, 42; Thyroxin, 43; Functions of the Thyroid, 45; Metabolism, 47; Detoxication, 55; Circulation, 57; Sexual Development, 58; Interglandular Equilibrium, 62; Emotional Mentor, 69; Conclusions, 71.

CHAPTER III

PATHOLOGY OF EXOPHTHALMIC GOITER 73

The Thyroid, 73; The Thymus, 76; Parathyroids, 76; Pituitary, 76; Suprarenals, 77; Nervous System, 77; Heart, 78; Orbits, 78; Pancreas, 78; Spleen and Lymphatics, 78.

CHAPTER IV

PATHOGENESIS OF EXOPHTHALMIC GOITER 80

(A) *Predisposing Factors*, 85; Geographical Distribution, 85; Heredity, 85; Age, 86; Sex, 86; Race, 87; Iodine Basedow, 67; The Infections, 88; Miscellaneous, 90; (B) *Exciting Factors*, 91; Summary of Ideas, 91; Theory of Intestinal Toxemia, 94; Neurogenic Theory, 96; Sympathetic Theory, 103; Thymus Theory, 105; Adrenal Theory, 108; Parathyroid Theory, 109; Pituitary Theory, 109; Gonad Theory, 110; Moebius or Hyperthyroidism Theory, 111; Dysthyroidism, 112; Pluriglandular Theories, 113.

CHAPTER V

SYMPTOMATOLOGY OF EXOPHTHALMIC GOITER 115

Acute Basedow's Disease, 115; Chronic or Usual Type, 117; Exophthalmos, 118; Tremor, 118; Vagotonia and Sympatheticotonia, 119; Hyperthyroidism with Hypothyroidism, 121; Basedow "Fruste," 124; Secondary Basedow, 128; Artificial Basedow, 129; Circulatory System in Exophthalmic Goiter, 130; Heart, 132; Blood Vessels, 138; Blood, 140; Thyroid Gland in Exophthalmic Goiter, 143; Primary, Hyperplastic Goiter, 143; Inspection, 146; Auscultation, 147; Nonhy-

PAGE

perplastic Goiter, 147; Simple or Nontoxic Goiter, 147; "Secondary Basedow" or "Basedowified" Goiter, 148; Thyroiditis, 150; Carcinoma of the Thyroid, 151; Syphilis of the Thyroid, 153; Tuberculosis of the Thyroid, 153; Intrathoracic Goiter, 154; Accessory Thyroid Goiter, 154; Eyes in Exophthalmic Goiter, 155; Exophthalmos, 155; Exophthalmos from Other Causes, 158; Stellwag's Sign, 159; Dalrymple's Sign, 160; Von Graefe's Sign, 160; Moebius' Sign, 160; Kocher's Sign, 161; Tremor, 161; Ulceration, 161; Jellinck-Teillais Sign, 162; Nystagmus, 162; Difficulty of Everting the Upper Lids, 162; Ophthalmoscopic Changes, 163; Optic Atrophy, 163; Vision, 163; Nervous System in Exophthalmic Goiter, 163; Tremor, 163; Temperament and Disposition, 168; Miscellaneous Nervous Phenomena, 170; Psychoses, 171; Gastrointestinal Tract in Exophthalmic Goiter, 173; Cutaneous Symptoms in Exophthalmic Goiter, 175; Respiratory System in Exophthalmic Goiter, 178; Genitourinary Tract in Exophthalmic Goiter, 181.

CHAPTER VI

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS 185

Simple or Nontoxic Goiter, 187; Secondary or "Basedowified" Goiter, 187; Neurasthenia, 187; Hysteria and Hysteroneurasthenia, 188; Nervous Indigestion, 188; Pulmonary Tuberculosis, 188; Paroxysmal Tachycardia, 189; Angina Pectoris, 189; Addison's Disease, 189; Symptomatic Anemia, 189; Septic Endocarditis, 190; The Psychoses, 190; Diabetes Mellitus, 190; Hypothyroidism, 193.

CHAPTER VII

SHELL SHOCK (?) IN SOLDIERS 195

A Misnomer, 195; Goiter in Armies, 195; Graves' Disease, 196; Study of Thyroid in Recruits, 197; Soldier's Heart, 199; Conclusions, 202.

CHAPTER VIII

DIAGNOSTIC TESTS IN EXOPHTHALMIC GOITER 206

Goetsch Test, 206; Pituitary Test, 207; Basal Metabolism, 208; Hyperglycemia Test, 208; Thyroid Extract Test, 209; Digitalis Test, 210.

CHAPTER IX

COURSE AND PROGNOSIS OF EXOPHTHALMIC GOITER 211

Mortality of Graves' Disease, 212; Intrinsic Factors Influencing Course and Prognosis, 215; Age and Sex, 215; Previous Condition, 215; Digestive System, 216; Heart, 217; Nervous System, 217; Severity and Duration, 218; Complications, 218; Social Conditions, 219; Cooperation of Patient, 220; Extrinsic Factors Influencing Course and Prognosis, 221; Early Diagnosis, 221; Nature of Treatment, 222; Duration of Treatment, 225; Environment during Treatment, 226; Personality of Physician, 228.

PAGE

CHAPTER X

THE NONSURGICAL TREATMENT OF EXOPHTHALMIC GOITER 229

Introduction, 229; Prophylaxis, 232; Hygienic, 245; Rest, 245; Exercise 249; Climate, 251; Hydrotherapy, 252; Gastrointestinal Hygiene, 254; Mental Hygiene, 254; Dietetic, 255; Importance of Careful Scientific Feeding, 255; Quantity of Food, 256; Increase in Weight, 258; Digestive Disorders, 259; Frequency of Feeding, 260; Nature of Dietary (Flesh vs. Non-Flesh Food), 265; Diet Lists, 266; General Medicinal Treatment, 270; Thyroid Extract, 270; Parathyroid Extract, 271; Pituitary Substance, 272; Tethelin, 273; Thymus Substance, 274; Suprarenal Gland, 274; Ovarian Extract, 274; Pancreatic Extract, 275; Lactic Acid Ferments, 275; Vaccines, 275; Serum Therapy, 276; Lecithin, 277; Quinine, 279; Arsenic, 281; Arsenic and Mercury, 281; Iron, 281; Iodine Therapy, 281; Intestinal Antiseptics, 285; Sodium Phosphate, 285; Sodium Salicylate, 285; Oil Injections, 285; Dechlorination, 286; Calcium Salts, 286; Belladonna and Atropine, 286; Digitalis, 286; Nerve Sedatives, 287; Ichthyol, 288; Local Treatment, 291; Medicinal, 292; Miscellaneous, 294; Electrotherapy, 299; X-ray Treatment, 300; Radium, 307; Galvanism, 308; Static Electricity, 309; Leduc's Current, 310; D'Arsonval's Current, 311; Psychotherapy, 311; The Mind in Medicine, 312; The Ego in Health and Disease, 314; Sympathy and Affection, 317; Sexual Instinct and Balance, 321; Psychotherapeutic Influences in Treatment of Exophthalmic Goiter, 324; Personality of Physician, 325; Correction of Social Environments, 327; Rest and Exercise, 329; Laughter, 330; Music, 334; Reading, etc., 337; Miscellaneous Esthetic Recreation, 339; Maintenance of Patient's Mental Equanimity, 339.

CHAPTER XI

A FEW CASE HISTORIES 343

Case Histories of Nonsurgical Cures, with Their Treatment, 343.

CHAPTER XII

CONCLUSIONS ON THE TREATMENT OF EXOPHTHALMIC GOITER 381

Why Exophthalmic Goiter Is Not a Surgical Disorder, 381; Fallacy of Surgical Premises and Procedures, 383; Surgical Complications and Sequelæ, 384; Surgical Statistics and "Cures", 386; Opinions of Thyroid Surgeons Implying Doubt of Efficacy of Surgical Procedures, 387; Opinions of Internists: Exophthalmic Goiter is Permanently Curable by Nonsurgical Procedures, 397; Author's Conclusions, 399.

APPENDIX

ARTICLES ON EXOPHTHALMIC GOITER BY THE AUTHOR 401

EXOPHTHALMIC GOITER

INTRODUCTION

Some years ago, as I was about to conclude my morning office hours, a man who was a stranger to me was ushered into my presence for treatment. As I beckoned him to a seat, it was seen that he was too weak to be about,—almost falling into the chair behind him. His physiognomy was a picture of a combination of fright and anxiety; his staring eyes seemed almost to pop out of their orbits, and as he waited a moment to rest himself, it was evident that his condition was one of impending heart failure. His skin was moist and dusky, the lips and conjunctivæ were almost blue, and as this miserable creature was about to address me, I noticed that his whole body was vibrating with the rapid cardiac cycles. On closer inspection, the carotids and jugulars were seen to throb violently, and even the thyroid which was moderately enlarged, was also busily engaged in the display of the circulatory embarrassment by throbbing synchronously with the great vessels of the neck.

"Doctor, I came to see what you can do for me," he said in a hoarse, faltering tone. "I was told that I have just a little while to live, but I don't want to die. I have a wife and six children to support, and I want to live a while longer if possible." Here he paused a moment to gasp for breath, and then resumed: "You see, my sickness began fifteen months ago, but they haven't been able to help me. Instead, I am getting worse,—I can hardly get about." He emitted a loose cough and continued: "I was treated in the wards of three hospitals for weeks at a time, and in each place, finding that they could not help me, they wanted to operate on my neck. Somehow, I was afraid; I had no confidence in the operation. Then I spent all the spare money

I had consulting specialists, nerve specialists and others, until now I am penniless and worse than ever. I wish I had permitted them to operate on me at first. Perhaps it would have cured me, but they tell me that it is very risky to operate now, as my heart is leaking." He stopped once more, and I did most of the talking from that moment on. The history revealed the fact that about a year and a half before, he had been badly frightened and shortly afterward found himself very nervous and unable to sleep. Soon he began to suffer with continuous precordial distress, and at times this was so severe as to make him feel as though his heart were gripped within the jaws of a vise. At the same time, though rapidly losing in weight and strength, he found it necessary to increase the size of his collars, as the anterior aspect of his neck was becoming swollen. According to the patient's history, the complete Basedowian syndrome made its appearance within four months after the occurrence of the fright. Physical examination revealed, in addition to the cardinal symptoms of exophthalmic goiter, a badly dilated heart in a state of *delirium cordis,* with double mitral and tricuspid murmurs. There was edema of both legs to above the knees, a beginning ascites and an increase in size of the liver and spleen due to passive congestion. It was evident that the heart was losing compensation very rapidly, and that treatment would be of no avail, as it was apparently too late. I was about to send him to a hospital when he pleaded, "Don't send me to a hospital; I have been in three of them, and this is the result. Just do what you can for me. I know there is no hope, but I place myself under your care and promise to obey all your orders. I will not go anywhere but home; I want to live or die with my family."

We often meet with sad cases in our professional experiences, but here was one which touched the tender cords very much indeed, and also made me wish that I was out of town that day.

"I can make no promises," I remarked. "But since you insist that I do something, we'll try." I then outlined a regime of dietetic, hygienic, and medicinal treatment for the man and ushered him out of the office in the care of the relative who had brought him. Then I tried to forget the incident.

One week later, to my surprise, he again appeared in my office, and I found that his condition was far from worse, although I could not detect any real improvement. He continued to make weekly visits, and before two months had elapsed, the patient stated emphatically that he was better. Physical examination at that time disclosed the total disappearance of edema and ascites, and the restoration of the liver and the spleen to their normal size. Thus enthused by the patient's optimism and the improved clinical picture, I soon found that he was regaining his health. Slowly but surely, week after week, the heart was observed to contract to within its normal limits, the murmurs at the same time becoming less and less audible until, six months after this treatment was begun, the cardiac apex was in the fifth left interspace in the mammary line, and no murmurs were audible. Concomitant with this circulatory restoration there occurred a gradual improvement of all other subjective and objective phenomena characteristic of an advanced case of exophthalmic goiter. The patient's nervous system became normal, his strength was restored to the degree of enabling him to resume his usual duties so that he could support his family; there was a gain of 30 pounds in weight which changed his appearance from an emaciated but bloated invalid—bloated from edematous infiltration—to a robust, plethoric, muscular-looking individual, feeling as well as he had ever felt in his life. Within one year following the institution of the treatment, the exophthalmos had entirely disappeared, the thyroid gland was restored to its normal size, and he was discharged cured. At this writing he is conducting a large ice-cream manufacturing business and is doing at least one strong man's physical labor each day.

This case was the starting point from which a series of complete nonoperative cures of Graves' disease resulted; it was also the beginning of a series of papers relating these experiences and pointing out the futility of surgery in general in the therapeusis of the disease. It was the beginning of a plea to the skeptical members of the profession, especially our friends the surgeons, to be more conservative in their thoughts and decisions when dealing with a hyperactive thyroid gland. My convictions and position in the matter became firmly crystallized when I found myself called upon to treat nonsurgically several patients who, after thyroidectomy had proved a failure, had the courage to seek aid from still another doctor.

The art and science of medicine, as all other arts and sciences, is fraught with periods of fads, which latter constitute the *comme il faut* for the profession at large during a variable length of time. Time was when blood-letting was considered the panacea for almost every disease; this procedure has now, with few exceptional indications, gone into disrepute as a cure-all. Not many decades ago, wounds were considered exactly right when pints of pus issued from them; now our patients are looked upon as infected in the presence of pus, and we endeavor to cure traumatic and surgical wounds by the clean first intention method. Again, the greater the fever in a patient, the more he was deprived of water and fresh air; modern medicine recognizes that plenty of water and fresh air are the greatest aids in combating febrile affections. Only recently, the profession at large has come to realize the fallacy of the indiscriminate removal of tonsils. The propaganda for reform in this direction is based upon the logical opinion that tonsils have their functions just as the thymus and the other lymphatic glands of the body; that enlarged tonsils, provided they are not diseased and there is no marked respiratory obstruction, serve the purpose among other functions of compensating for a deficient glandular activity elsewhere; and that their removal is not only an unnecessary procedure, but physiologically erroneous. And so, as we survey the periods in medicine, we find repeated examples of theories and procedures formerly considered proper, but which soon give way to other theories and procedures in accordance with further physiologic and clinical observation. Arts and sciences, as well as men, are susceptible to "ruts" into which they will fall and there remain for a much longer period than subsequent developments and conditions justify, simply because it is a somewhat painful procedure requiring considerable effort to come out into the open and accept suddenly presented views entirely at variance with habitual methods.

The most important disease in which a controversy of this sort is now enacted is exophthalmic goiter. For many years the majority of medical men have considered this disease as one belonging to the operating table for relief. Many theories, ingenious and otherwise, have been promulgated to suit the therapeutic conclusion, and thousands upon thousands upon thousands of cases have been so treated. Successfully? Yes. That is, the patient usually recovers *from the operation.* But what about cure of the disease for which operation was attempted? Ah, there's the rub! The goal in the treatment of exophthalmic goiter is to secure a cessation of thyroid intoxication, *i. e.,* permanently to arrest the processes which produce the saturation of the blood with thyroid substance, and the repair of whatever damage there has been wrought in the patient's organs and functions during the entire course of the disease. This surgery sometimes appears to accomplish for a brief few weeks' duration, but as a general rule, rarely if ever succeeds permanently to accomplish. On the contrary, many instances occur in which, far from a diminution of thyroid intoxication on leaving the operating table, the patient's system is more than ever saturated with thyroid substance.

The increased attention given by the medical profession to the subject of endocrinology, especially to the study of the thyroid gland, is not without cause. What is the rôle of the thyroid gland? The answer to this question would probably mean a more satisfactory definition of the term "Life," so great would be the discovery. It would mean a practical solution of all problems relating to the mysterious bodies classified as endocrine organs; the revelation of Nature's treasure house of information concerning the etiology and successful cure of many physical and mental diseases which have been puzzling the medical profession since the beginning of its history. What a glorious victory over many of the processes hindering longevity and happiness this would be!

Various factors are responsible for the undoubted increase in the number of cases of Graves' disease during the past generation. The increased strenuosity of modern life, productive as it is of great numbers of hysterical individuals, neurasthenics, nervous dyspeptics, and the like, is also by its profound effect upon the circulatory and nervous systems and especially upon the emotional balance, a potent factor in the etiology of hyperthyroidism. Again, the recent world conflict has brought to the attention of the medical profession the revelation of that which was vaguely suspected for a long time, that a sudden change from one's accustomed environments to an atmosphere of complete subordination and servility in the presence of the most intense apprehension and danger to life and limb, as experienced by the raw recruit in the trenches, is not only capable of increasing the activity of the thyroid gland, but has brought into existence thousands of instances of Graves' disease in varying degree in men who probably would have been normal at least so far as the thyroid gland is concerned; and it is this picture of tachycardia, palpitation, tremor, throbbing thyroid, slight exophthalmos, extreme emotionalism, marked prostration, and other minor manifestations, which is frequently termed shell shock. Yet a third factor may explain the increased number of cases of hyperthyroidism in recent years, and that is the tendency of the profession to change from homogeneity, as represented by the general practitioner, to heterogeneity, as represented by the specialist. In other words, as the various branches of medicine become more clearly defined into the various specialties, refinements in diagnostic methods are more apparent, and diseases which have heretofore been erroneously diagnosed are now recognized as indisputable entities. In passing, it may be remarked that since endocrinology is such a broad field of endeavor and since there are thousands of cases of Graves' disease still erroneously diagnosed because of the elusiveness or vagueness of the clinical picture, and finally (and this is perhaps the most important reason), since the surgeons and internists are still at odds with respect to whether surgical or nonsurgical treatment should be given the preference in the management of hyperthyroidism, the study of the diseases of the endocrine organs and the looming forth into the arena of the endocrinologist should be encouraged and supported by the profession now, more than ever before.

Now a word about the patient himself. In a scientific work, especially a medical treatise, the writer and often the reader too, will become so thoroughly absorbed in the speculative phases of cause and effect in phenomena discussed,—so keenly absorbed in postmortem examinations and the pictures of microscopic sections, that the living human being—the patient himself—is practically forgotten. This is a mistake not only in the abstract moral sense, but is quite an erroneous attitude even from the viewpoint of scientific duty, since we must all concede that the first and foremost obligation of the physician is to assist humanity and ease its mental and corporeal afflictions. To have *everything* subserve pathologic investigation and scientific precision in diagnosis is to concur with the surgeon in the time-worn assertion: "The operation was very successful, but the patient died."

Not that we must not be enthusiastic and eager and accurate with strictly scientific phases of our work, for this would deter progress and defeat the purpose of medicine itself. We *must* be scientists, but we *must* also be humanitarians and treat the patient as well as the disease. Especially is this true in a disease like exophthalmic goiter, where the nervous system, especially the psychic centres, are undergoing a state of turmoil. To treat this patient scientifically *only* is to court failure and in many instances lose the patient. The patient cares not a whit what terms you employ for this or that sign or symptom; he is not even keenly desirous of knowing the name of the disease. But he *is* anxious to become restored to former health, utility, happiness, and above all, to his former position in his circle of relatives and friends.

Since in exophthalmic goiter the mind is quite as sick as the body (and sometimes more so) and since as scientists we are quite aware of the influence of the mind on the body and vice versa, it is obvious that to treat the body alone is not the successful method of procedure, no matter how logically, how consistently or carefully this is attempted. If we are to transform our sick patient into a well friend and send him back to enter the ranks of striving, hopeful, useful humanity, imbued once more with the joy of life, we must combine mental treatment,—*psychotherapy*—with our other measures. And here we again come to our own when we conclude that we must employ *scientific* psychology with other *scientific* therapeutic measures if we would do our duty and successfully assist our charge promptly to win the battle of life and health. It is for these reasons that the author has seen fit to include a section on the psychotherapeutic treatment of exophthalmic goiter, which he considers of vital necessity in the successful treatment of the disease.

CHAPTER I

ANATOMY

The thyroid gland is reddish in color, consisting of two lateral lobes and a connecting isthmus which unites them near their lower ends. The organ is somewhat convex on its outer aspect and clasps the upper end of the trachea, extending upward for some distance upon each side of the larynx.

The thyroid is a ductless gland, varying greatly in size and shape in various individuals. According to McCarrison, in the absence of other factors, an increase of three-fourths to one inch in the circumference of the neck represents a doubling of the volume of the thyroid gland, a further increase of three-fourths to one inch a tripling, and a still further increase of one-half to three-fourths of an inch a quadrupling of the gland's volume. These figures he considers approximately correct for necks whose normal circumference is 13 to 16 inches. In females and in children it is relatively larger than in the adult male; it varies in size with the degree of nutrition of the patient. During menstruation and pregnancy, it frequently increases in size. Moreover, in certain families (through heredity) and in certain parts of the world, the normal thyroid may be considerably larger than the standard herein mentioned. No organ of the body is more subject to variations in size, shape, blood supply, structure and function than is the thyroid gland. Is it any wonder that its study is the subject of increasing interest from year to year?

Shape and Relations.—Each lateral lobe is somewhat conical or pyramidal in form, with its broad end below, measuring approximately 2 inches in length, an inch in breadth, and an inch in thickness near its middle. Its apex rests upon the ala of the thyroid cartilage; the base extends downward upon the side of the trachea to the fifth or sixth tracheal ring, about three-fourths of an inch above the sternum. Its superficial surface is somewhat flattened, covered by the pretracheal layer of cervical fascia, which latter forms the sheath for the gland, connecting it so firmly to the surrounding parts and to the trachea as to follow the movements of the latter. It is also covered by the sternothyroid, sternohyoïd, and omohyoid muscles. Its deep surface adapts itself to the sides of the trachea, to the cricoid cartilage, and to the inferior cornu and adjoining part of the surface of the ala of the thyroid cartilage. Its posterior border extends backward touching the esophagus and pharynx and overlapping the carotid sheath (containing the common carotid artery, the pneumogastric nerve and the internal jugular vein), the inferior thyroid artery and the recurrent laryngeal nerve. It must be remembered that the parathyroid glands are also in relation here. The inferior thyroid arteries enter the lateral lobes from the inner side and the superior thyroid arteries from the antero-external. The middle cervical sympathetic ganglion is behind. The inferior laryngeal nerves lie at its inner surface, the left one being in actual contact with the thyroid, and the right one usually very close to it.

The isthmus of the thyroid is a band of varying width, (from one-fourth to three-fourths of an inch), lying over the second, third, and often the fourth tracheal rings. The isthmus is sometimes absent, or, it may give rise to the so-called pyramidal process, and occasionally so cover the cricoid cartilage as to render the performance of a superior tracheotomy a difficult procedure. Rarely is the isthmus separated from the lobes, forming a sort of lobe by itself.

The pyramidal or middle lobe of the thyroid is inconstant, occurring in probably 40 per cent of cases, and is regarded as the vestige of the thyroglossal duct. The typical pyramidal lobe reaches the hyoid bone, to the body of which it is attached either by muscle or ligament. It is attached by its base to the upper border of the isthmus or to the adjacent left lateral lobe, hence it is found more frequently on the left side than on the right.

A strand of tissue, partly fibrous, partly muscular, called the *levator glandulæ thyroidæ,* connects the capsule to the hyoid bone. Median bands, described as suspensory ligaments, connect the capsule to the cricoid and thyroid cartilages. A lateral ligament passing backward and upward to the first ring of the trachea, to the cricoid, and perhaps to the inferior horn of the thyroid cartilage is fairly well defined.

Structure.—The thyroid body corresponds in its development with other compound alveolar glands excepting that there are no excretory ducts and there are peculiarities in the structure of its terminal compartments. The closely applied thin capsule of connective tissue gives off septa from its deep surface which subdivide the organ into lobes and lobules. From the septa separating the lobules fine lamellæ proceed, which form the subdivisions or boundaries of numbers of closed vesicles or alveoli of varying size and shape, each lined by a layer of cubical or columnar epithelial cells, most of them containing a viscid semifluid colloid material. In the fibrous tissue, septa traverse the blood vessels of the organ, whilst the capillary network is arranged on the outer surface of the vesicles. Numerous lymphatic vessels, frequently containing colloid material, arise external to the alveoli (Baber).

Histology.—The thyroid is a ductless gland, the terminal subdivisions (acini) of which vary from .05 to .2 in size depending upon the degree of distention by secretion. They are lined with a single layer of polygonal cells, the height of the latter varying with the degree of distention of the follicle. A distinct basement membrane is lacking, the cells resting upon a somewhat condensed stratum of surrounding connecting tissue. In the zone of each cell, next the sac, there is usually found a varying number of highly refracting granules, the probable source of the colloid secretion. The cells forming the acini may be divided into (*a*) "principle" or "chief" cells which are the most numerous, containing a variable quantity of fine granules, and (*b*) "colloid" cells, which are somewhat more opaque and granular. These types are not in reality distinct, as one form readily merges into the other during physiologic activity, and the colloid cells constitute those which are loaded with material derived from the granules ready to be discharged into the lumen of the acinus. "For the majority of the thyroid cells, the secretion affects the *mecronine type.* This means that a part only of the cell is used by the secreting process. Once elaborated, the secretion is evacuated into the alveolar lumen by the breaking open of the nuclear membrane; then the cells regenerate and become 'chief cells' ready to start over the secreting cycle. In numbers of other instances, however, the secretion affects the *holocrine type.* In these cases the whole cell is used for colloid material. Nothing remains afterward, the whole cell is destroyed" (Crotti).

Blood Supply.—Regarding the vascularity of the thyroid gland Mayo remarks: "No other human organ in the body is so well provided with a blood supply. In proportion to its weight it receives twenty-eight times as much blood as the head, and all the blood in the body passes through it as it does through the brain, once every hour. It is known to be five and a half times more vascular than the kidney. While the lymphatics are numerous, those leaving the gland are small as compared with its wonderful supply, apparent activity, and production of secretion. It is probable, however, that this secretion is delivered into the veins by short lymph spaces throughout the gland itself." Four large vessels, and occasionally a fifth, convey the blood to the thyroid body. Two superior thyroid branches spring from the external carotid arteries. Each of these divides at the apex of the lateral lobe into three branches for its supply. Two inferior thyroid branches from the thyroid axis of the subclavian artery distribute their terminal branches to the basal portions and deep surfaces of the lateral lobes. The occasional artery is the *thyroidea ima,* a branch of the innominate, which ascends upon the trachea to reach the isthmus of the thyroid body. The thyroid arteries anastomose freely with each other.

The veins which drain the blood from the thyroid body and which are without valves, are still more numerous. They are three in number on each side, viz., the superior and middle thyroid veins, which join the internal jugular; and the inferior thyroid, which descends in front of the trachea and joins its fellow on the opposite side to form a large common stem which opens into the left innominate vein. Numerous large veins ramify on the surface of the organ and lie in grooves in its substance. It is from this plexus that the inferior thyroid veins take origin.

The Lymphatics.—The lymphatics begin with the organ as perifollicular lymph spaces; from these plexuses follow the interlobular septa in their course to the exterior, where they constitute a superficial plexus from which the lymph passes in all directions. Some run upward from the isthmus to small lymph nodes in front of the larynx, some from the sides to the deep glands about the internal jugular, and some from the isthmus and adjacent parts downward to pretracheal lymph nodes.

The Nerve Supply.—The nerve supply is derived from the superior, middle and inferior ganglion of the cervical sympathetic, and the superior laryngeal branch of the vagus. Some observers include the inferior laryngeal nerve. The various nerve filaments are distributed to the secreting epithelium, to the walls of the blood vessels, to the capsule and its ramifications. The secretion of the gland is under the control of the filaments from the cervical sympathetic, and Cannon, quoted by McCarrison, states that as a result of experimental stimuli the secretion issues as promptly as in five to seven seconds. "The same observer has shown that when the phrenic nerve is joined to the peripheral portion of the cervical sympathetic in the cat and the thyroid is thus continuously stimulated as the animal breathes, this operation results in tachycardia, increased excitability, loose motions, exophthalmos on the operated side, great increase in the metabolism, and in some cases an increase in the size of the adrenals'' (McCarrison).

Accessory Thyroids are small detached bodies consisting of tissues similar to the thyroid proper and are occasionally found in the neighborhood of the lateral lobes or about the hyoid bone in the midline. They are sometimes found in the neighborhood of the tongue, and according to d'Aintolo (quoted by McCarrison) they may even be found under the maxilla behind the pharynx or esophagus in the vicinity of, or more rarely in the larynx and trachea near the cricothyroid and aorta and in the mediastinal regions. Most of these are remnants of the median thyroid diverticulum from the primitive pharynx, sometimes represented by the thyroglossal duct. ''This passed originally in front of the hyoid bone, thus accounting for suprahyoid and prehyoid accessory thyroids. Those behind and below the hyoid are probably the result of an upward or downward growth from the primary diverticulum'' (Piersol).

Remarks.—The thyroid, as a ductless gland with an internal secretion, is one of the most important organs, for its congenital absence, deficiency, operative removal or hyperactivity give rise to cretinism, myxedema, cachexia strumipriva, and Graves' disease respectively,—all evidences of most marked interference in metabolic balance. The vast blood supply with the complex capillary network coming in practically direct contact with the secreting cells, the equally plentiful plexus of veins quite as closely related with these secreting units, and the copious lymph supply bathing the cells,—all these speak for the thyroid secretion as occupying a primal position, to say the least, among the body juices.

The thyroid blood supply is greater than in any other organ. ''In proportion to its size, it receives more than five times as much blood as the kidneys, while nearly as much passes through its arteries as through the internal carotid and vertebral to the brain. Vasomotor dilatation, therefore, is capable of giving rise to rapid swelling of the gland'' (McCarrison). It can readily be seen, then, that where there is a frequent physiologic hyperactivity with concomitant increased vascularity of the thyroid as in frequent pregnancies, unusual types of menstruation, or even repeated nervous strain (emotional excitement, shock, etc.), the thyroid is apt not only to remain enlarged, but also to become chronically hyperactive.

Any stimulus to the sympathetic nervous system, especially the cervical, gives rise to increased thyroid activity; and frequently repeated stimuli lead sooner or later to a chronicity of effects expressed by the syndrome observed in exophthalmic goiter. Irritation of the median cervical sympathetic ganglion by an enlarged simple goiter or other agent may likewise lead to the syndrome; the differential diagnosis between this picture of events and that of true hyperthyroidism is difficult.

With respect to the anatomic relations, the following may be remarked:

(*a*) The sheath enclothing the thyroid connects it to the neighboring parts so firmly that it rises and falls with the movements of the trachea. Hence all thyroid enlargements must of necessity follow the movements of the trachea.

(*b*) An enlarged gland occasionally insinuates itself between the carotid artery and internal jugular vein, resulting in interference with the circulation of these vessels. According to Burns, in rare cases the isthmus is found between the trachea and esophagus, and this may give rise to dysphagia.

(*c*) The close relation of the parathyroid glands is the cause of their occasional accidental removal during thyroidectomy with resulting tetany; injury to the recurrent laryngeal nerve directly through operation or indirectly through contraction of scar tissue is not uncommon, leading to paralysis of the vocal cords.

(*d*) In the event of its enlargement, the ultimate relationship of the thyroid gland with the surrounding structures may result in

(1) Headache, vertigo, epistaxis and cyanosis in consequence of pressure upon the carotid and jugular veins. Pressure upon the pneumogastric nerve may give rise to phenomena varying with the degree and constancy of the irritation.

(2) Dyspnea occurs with varying frequency in statistical records and occurs in consequence of the resistance of the underlying muscles and the pretracheal cervical fascia to the gland. This symptom is most marked in instances where the isthmus is greatly involved, or where the latter lies between the trachea and the sternum. Occasionally, a unilateral enlargement of the thyroid gland may give rise to dyspnea by the displacement of the trachea to one side.

(3) Dysphagia may result from pressure upon the pharynx or the esophagus and is more common in left-sided goiters, for anatomic reasons.

(4) Dysphonia with hoarseness, and rarely aphonia may result from pressure upon the recurrent laryngeal nerve. In my experience, it has often been difficult to distinguish between the dysphonia of nerve irritation and that occasioned by the congestion due to pressure upon the trachea.

(5) Pulsation and bruit may occur in varying degree, depending upon (*i*) the degree of pressure exerted upon the carotid artery by the enlarged gland; (*ii*) the extent of the increase in the vascularity of the organ (increase in caliber and number of blood vessels), or both.

A note of caution should be sounded with respect to local manifestations. If the patient is not young and there is pain and tenderness referable to the thyroid substance and the gland is found to be somewhat cyanotic in places and nodular, the skin closely adherent to underlying structures, look out for malignant changes!

(*e*) Accessory thyroids may become hyperactive, leading to typical symptoms of Graves' disease without any perceptible enlargement of thyroid proper. Such cases often explain Graves' disease without goiter and are frequently undiagnosed until late in the disease.

The Parathyroid Glands

Though it is not our purpose to discuss these glands in detail, the intimate relationship which the thyroid gland bears to the parathyroids renders a brief mention of these bodies necessary for the sake of completion.

Relations.—These organs, formerly mistaken for either accessory thyroids or for lymphatic nodules, are small elliptical masses, lying in more or less close relationship with the lateral lobes of the thyroid and separated from them by the capsule. Usually there are four, one near each pole of the lateral lobe. Posteriorly, the lower pair is in close proximity to the branches of the inferior thyroid artery and recurrent laryngeal nerve. According to Welsh, the appearance of the superior pair is more constant than that of the inferior, lying on the posterior wall of the esophagus about the level of the lower edge of the cricoid cartilage, immediately internal to the posterior border of the lateral lobe of the thyroid, and in front of the prevertebral fascia.

Structure.—The parathyroid bodies are composed of epithelial cells which in structure bear a close resemblance to the anterior lobe of the pituitary body (Welsh). In both organs colloid-containing alveoli are occasionally found. Schafer believes that the parathyroids correspond in structure to the immature and undeveloped thyroid.

Blood and Nerve Supply.—The arteries spring from those supplying the thyroid. Concerning the veins, lymphatics, and nerves of the parathyroids, not much is known, but very likely the nerve filaments are derived from the cervical sympathetic.

The knowledge of the anatomy of the parathyroids is of great importance in thyroid surgery in view of the fact that their accidental removal leads to death from tetany.

Development

"The thyroid is developed from three *anlagen,* an unpaired median and two lateral. The *median anlage* appears in the embryos of from 3-4 mm. as an epithelial outgrowth from the anterior wall of the primitive pharynx in the region of the second visceral arch, and therefore in close relation with the posterior part of the tongue. At first possessed of a narrow lumen, the evagination soon loses its cavity and becomes a solid pyriform mass, which for a short time is connected with the pharyngeal wall by a delicate epithelial strand. Usually the latter soon disappears and the isolated median thyroid, which meanwhile rapidly increases as a bilobed mass, passes to the lower level of the lateral *anlagen.* The position of the primary outgrowth is later indicated by the depression of the tongue, the *foramen cecum,* just behind the apex of the V-row of the circumvallate papillæ. Occasionally the evagination persists, and then forms the *thyroglossal duct,* a narrow tube extending for a variable distance from the tongue towards the thyroid body. The *lateral anlage* appears on each side as an epithelial outgrowth from the ventral wall of the fourth pharyngeal furrow, the minute pocket soon becoming transformed into a sac, which early separates from the pharynx. The three primary rudiments grow ventrally, and later, in embryos of about 20 mm., join to form the definitive thyroid surrounding the larynx; of the three, the median anlage contributes the most important part of the thyroid body. Comparative embryology emphasizes the significance of the median anlage as the thyroid proper; indeed, all participation of the lateral rudiments in forming the organ in certain animals is denied (Verdun). The histogenesis of the thyroid includes two stages, the first being distinguished by numerous cylindrical epithelial cords from which grow out lateral branches. The second stage witnesses the fusion of these epithelial cords into a network the meshes of which are occupied by vascular mesoblastic tissue. During the third fetal month the epithelial reticulum breaks up into masses corresponding to the follicles of the thyroid. These gradually acquire a lumen around which the cells become arranged to constitute the epithelial lining of the compartments in which later the characteristic colloid substance is secreted. The thyroid agrees with the parathyroids and the thymus in originating from the walls of the primitive pharynx and, likewise, in deviating in its later development from its primary correspondence to a typical gland. They are remnants of the median thyroid diverticulum from the primitive pharynx, sometimes represented by the thyroglossal duct. This passed originally in front of the hyoid bone, thus accounting for suprahyoid and prehyoid accessory thyroids. Those behind and below the hyoid are probably the result of an upward or downward growth from the primary diverticulum" (Piersol, "Human Anatomy").

CHAPTER II

PHYSIOLOGY OF THE THYROID

The chief difficulty encountered in the study of the endocrine organs is the fact that we are unable to secure precise laboratory data based on experiments on human beings. Most of our information on the subject is derived from animal experimentation, and while this is of undoubted value, it falls considerably short of absolute utility in the alleviation of human affections, so that the therapeusis of the endocrine diseases is based largely upon empiricism. In the thyroids of persons who have died of disease, the tissues are lacking in normal characteristics, and the study of them is unsatisfactory. Most reliable sources of information must of necessity be derived from conclusions deduced from a study of patients suffering with various types of thyroid abnormality, which deductions, though highly valuable, leave much for further investigators to explain.

Structure

With regard to its structure in general, C. H. Mayo states: "From the care with which nature has guarded its blood supply, the thyroid, weighing approximately but an ounce, is a gland the secretion of which is of the utmost importance; this we see proved in the vegetative type of animal existence which occurs in cretins who are born without this gland, or those who subsequently lose it—the myxedematous. No other gland in the body has been so well cared for in its circulation by nature as the thyroid. * * * With its four regular arteries supplied by various main trunks and the anomalies leading to greater circulation, nothing should interfere with it. The gland consists of a mass of alveoli or vesicles lined with a single layer of columnar cells. Having no ducts, it has been assumed that its secretion passes through the lymphatics or through the venous system as a hormone. There is no outlet for the interior of the vesicles, and the secretion of colloid accumulates here. It is evidently true that these cells deliver a secretion from their bases, and accumulations within the vesicles, should they ever leave them, are passed back through the cells as a filter."

According to R. R. Bensley, the secretion is indicated by the appearance of vacuoles in the outer poles of the cells. These contain a dilute solution similar to the colloid in the follicles. This is probably excreted directly into the vascular channels. The intrafollicular colloid is probably formed from the vacuoles in the outer pole of the cells. The stored intrafollicular colloid is no measure of the activity of the thyroid at the time of observation. This activity is indicated by the intracellular secretion.

The nerve supply, especially the secretory nerves of the thyroid, is a subject upon which reliable information is not obtainable. It was believed that the thyroid secretion depends upon the influences of the nervous system, especially from the cervical sympathetic filaments and the laryngeal branches of the vagus. However, it is well known that a variation of the blood supply of an organ is sufficient to account for changes of function without assuming nerve influences on the secretory cells. It is also known that chemic and biologic stimulants and depressants within the blood may influence glandular secretion without the medium of nerve influences. At present, with respect to the thyroid, the weight of opinion is seemingly in the direction of the belief that the degree of *vascularity* of the organ is the determining factor, as is believed by many to be the case with respect to the kidney, liver, and other organs. This is seemingly exemplified by the marked vascularity of the hypersecreting thyroid, a pathognomonic sign of Graves' disease, easily observable on palpation and auscultation.

Factors Governing Secretion

To confirm the assumption that the thyroid secretion is regulated by its blood supply, we need but note that "in the dog it is possible to graft an extra thyroid into the abdominal cavity and then to remove the original gland, when the second organ will assume the function necessary to the preservation of health. This was an important discovery, since it removed the ground for a prevalent opinion that the service of the gland was limited to the reflexes which it was supposed to originate. It had been thought that the gland affected the nutrition and general health by sending impulses along the nerves leading from it to the centers. A gland substituted for the native one and placed in a remote part of the body could not be in connection with the old afferent pathways, and whatever effect it must have, must be chemic in origin" (Stiles).

Manley and Marine, after making 289 autothyroid transplants in 141 rabbits, conclude that autotransplants "take" and grow, and the amount of growth is determined by the amount of thyroid removed and also by the administration of iodine or desiccated thyroid. The nerves are not necessary for normal growth or functional activity of the thyroid. The results with homografts are not so satisfactory, and the duration of the grafted tissue is modified by both the host and the tissue used for the grafts. These two factors may be quite independent, antagonistic, or helpful to each other. In the case of the thyroid, this reaction may be modified by iodine.

E. Krummer states that a thyroid graft to be successful must secure a good vascularization with good conservation of the follicular apparatus and particularly of the normal epithelial cells, both as regards form and relation to one another, and retaining the colloid substance in the center of these follicles or in the perifollicular lymphatics. Such a graft thus presents manifest signs of functional activity; but in order to appreciate the degree and usefulness of its internal secretion, we have but one conclusive proof, and this is the biological test. Krummer points out that the proof that normal internal secretory powers have been retained by a graft lies in its physiologic service to the organism. If an animal is thyroidectomized and successfully grafted and then dies in a state of thyroprivia following the extirpation of the graft, we are justified in assuming its endocrine value. We have found in our experiments that this biologic test parallels the anatomical examination. In summarizing, this author presents the following deductions:

1. "We have not observed any new formation of nerves in thyroid grafts.

2. "The reestablishment of the function of the graft has not been any better when implanted in the neighborhood of the pneumogastric or its branches than when made in any other part of the body.

3. "In spite of denervation, the graft by itself alone is able to satisfy the need of the organism (of the cat or dog) for the thyroparathyroid internal secretions.

"*Conclusion.*—Whatever may be the importance of the rôle played by the autonomic nervous system as the secretomotor nervous regulator of the thyroid body, the thyroparathyroid graft without any nervous connection is capable of furnishing the internal secretion which suffices to maintain health in both the dog and the cat. From a practical point of view attempts to enervate grafts are wanting in interest. Judging from the well-known fact of the interchangeability of thyroid extracts of man and of certain animals, what we have found in the dog and the cat has every good reason to be true in man."

The Thyroid Secretion

Colloid is the iodine-containing substance of the thyroid gland; the greater the amount within the organ, the greater the stored iodine. During active secretion, especially when an emergency demand is made, as in menstruation, pregnancy, emotional disturbances, shock and the infections, the thyroid secretion is thrown into the blood in greater quantities. At this time, there is an increased vascularity of the gland, and a gradual thinning and entrance of the colloid substance into the lymph spaces. When the emergency need is satisfied, the gland soon reaches the "resting" stage by the reaccumulation of colloid substance within its acini. McCarrison insists that a distinction should be drawn between the "thyroid secretion" and the "colloid": "the latter term ought to be restricted to the reserve store of iodine-containing material. It is necessary to realize that the stored-up colloid is no measure of the activity of the gland at the time of its examination. This activity is indicated by the degree of parenchyma hyperplasia and the amount of 'secretion' lying between the cells and in the lymph spaces."

The amount of colloid found in a thyroid gland is in inverse proportion to the amount of thyroid secretion thrown into the blood, and usually in inverse proportion to the degree of activity of the organ. In Graves' disease, in the newborn, in the infections and other conditions where an increased demand for thyroid substance is made, there is diminished colloid substance in the gland; this is due to a tremendously increased absorption of the thyroid secretion, in spite of the increased secretion by the organ. In other words, in the presence of an increased demand, there is an increase in the vascularity of the gland, an increase in secretion, a greatly increased absorption of thyroid secretion into the blood, *but a diminished retention within the organ.* So that, in exophthalmic goiter, although there is an increased output of the thyroid secretion from the gland, the reservoir capacity of the organ is reduced.

In addition to iodine, colloid contains phosphorus, sulphur, arsenic, bromine and various miscellaneous substances such as leucomains, cholin, lipoids, albumosis, xanthin, hypoxanthin, sodium chloride, calcium oxalate, lactic acid and other substances apparently not playing an important rôle.

Iodine Content

That iodine is a normal constituent of the thyroid has been known for more than a generation, and even now it is held by most observers that all thyroid products depend for their activity upon the contained iodine.

If it is true that every cell of the body depends for its proper metabolic activity upon thyroid secretion, and since this secretion (according to most observers) depends for its activity upon the contained iodine, then every cell, every tissue, every organ of the body contains iodine. The quantity of iodine possessed by the various structures depends upon many factors. The parathyroids contain the most, the thyroid next, and the other tissues of the body come next in order, depending upon their needs.

It has been found that the iodine within the normal gland exists to the extent of 2 per cent combined with a protein substance, and that generally speaking, the iodine content of the normal gland is the greatest, that of the colloid gland is less, the parenchymatous hypertrophic and hyperplastic gland containing the least. Each respectively contains approximately 2.5 mg., 1.5 mg., and 0.5 mg. of iodine per gram weight of dried gland.

In the fetal thyroid iodine is present in very small amounts and may rarely be absent. In pregnancy the iodine content of the thyroid diminishes as the time of parturition approaches unless the mother is fed iodine, which increases it in both the maternal and fetal thyroid (Marine).

Iodine content of the thyroid increases with an increase in iodine-containing food. Thus, in a vegetable dietary and in herbivorous animals, the iodine content is greater than in a flesh-containing dietary and in carnivorous animals.

A. Seidel and F. Fenger (quoted by Crotti) state that in the sheep, ox, and hog, there is a marked seasonal variation in the size of the thyroid and the iodine content; there exists about three times as much iodine in the thyroid between the months of June and November as between the months of December and May. "The glands were found to be larger in the months during which the lower iodine content was noticed."

Sex and age also influence the iodine content of the thyroid; in the female, the percentage is greater than in the male, in the extremes of age the thyroid content is lower than in middle life.

Residence seems to exert an influence on the iodine content; McCarrison states that the functional activity of the gland seems to increase with residence at increasing heights above the sea level.

The variations in functional activity of the thyroid in the normal experiences of human beings, *e. g.*, adolescence, menstruation, pregnancy, lactation, menopause, and the various emotions—all these bring about a variation in the iodine content of the blood.

Iodothyrin

In 1895, Bauman discovered that the iodine associated with the thyroid secretion exists in organic combination which he called iodothyrin. It contains about nine per cent of iodine and is the result of decomposition of the proteins with sulphuric acid. The iodothyrin so obtained is about 4 per cent of the total weight of the dried thyroid.

Iodothyroglobulin

In 1915, Oswald reported on the effect of the iodothyroglobulin on the circulation. It produces no alteration in blood pressure or pulse rate. But after intravenous injection of this substance, which Oswald calls the true secretory production of the thyroid, adrenin causes a rise in pressure which may be twice as high as before. This effect is manifest, however, only after a short latent period and persists for a considerable time, having been demonstrated after the lapse of one and a half hours. It is Oswald's belief, therefore, that iodothyroglobulin renders sympathetic endings oversensitive to the action of adrenin.

Thyroxin

In the Rochester clinic, Kendall has recently succeeded in separating the organic substance from the iodine-containing thyroid, from the balance of the gland. This he accomplished by destroying the proteins of the thyroid by means of boiling with a strong alkali which does not decompose the iodine-containing compound. By suitable treatment, he separated a pure, crystalline substance containing 60 per cent of iodine, its formula being $C_{11}\ H_{10}\ O_3\ NI_3$. The compound contains an organic nucleus called indol and oxygen, and is known as *thyroxin.* Its function is involved in the most fundamental processes of life, the production of energy.

In discussing the chemical physiology of thyroxin, Kendall draws the following conclusions:

1. By an alkaline alcoholic hydrolysis the thyroid proteins are broken into many simpler constituents, which by their solubility in acids is separated into two groups. Those constituents insoluble in acid are designated group A and those soluble, group B. No definite crystalline compound has been isolated from group B, but it appears to be composed of mixtures of amino-acid complexes. About one-half the total iodine in the thyroid proteins appears among the group B constituents. The nucleus to which the iodine is attached is unknown. By continued hydrolysis the group A compounds have been further separated, and the iodine-containing compound has been isolated in pure crystalline form, having a constant iodine content of 60 per cent.

2. Physiologic tests on animals and human beings have shown that no toxic effects can be produced by any of the constituents of group B. Group A constituents, however, produce the so-called hyperthyroid symptoms; increase in pulse rate, with tachycardia, increase of nitrogen elimi-

nation, with loss of weight, and increase in nervous irritability, etc. Further investigation showed that the production of these symptoms was proportional to the iodine content, that partial purification of A did not destroy the activity, and finally that the compound containing A-iodine produced these effects in all stages of purity up to and including the pure crystalline form.

3. The amount of the A-iodine compound necessary to produce symptoms is extremely small. One-half mg. (1-120 of a grain) per day produced marked effects in a cretin weighing 15k. The susceptibility of animals and man to this compound varies greatly, but the human being responds much quicker and to a far greater degree than the dog. Some form of tolerance for the compound is produced. In very small doses the A-iodine compound exerts a tonic effect and appears to be essential for normal growth and life.

4. Administration of A-iodine to man produces changes in the cardiogram.

5. Although B produces no toxic effects, it appears to possess physiologic properties in certain conditions of the skin.

6. The toxic properties of A are due to the isolated iodine-containing compound; and there appears to be no relation between activity and iodine in B.

"Kendall's work has furnished the only pure, crystalline compound ever separated from the thyroid, that possesses the same physiologic activity as the gland itself. This work places the investigation of the thyroid on a clear, chemical basis and has made it possible to study quantitatively the action of the thyroid hormone" (C. H. Mayo). Thyroxin is of such extreme potency that 1 mg. administered daily to a normal individual will produce toxic symptoms. It possesses all the properties of the dried thyroid gland. Kendall shows that thyroxin does not act on the nervous system directly, but on the tissue cells themselves. In other words, there is a direct intracellular effect throughout the whole body, acting as a catalytic agent, exchanging carbon dioxide for amino-acids, then returning to the thyroid without loss of iodine in a manner analogous to the intraorganic commerce of the hemoglobin. Kendall concludes, therefore, that all the effects produced by the thyroid are through its influence on metabolism, and the various clinical changes produced by thyroid secretion are due to an increase in cell activity throughout the whole body. The mentality is increased by the increased metabolism going on in the brain cells, the condition of the skin improves because metabolism within the skin cell is increased, and so on throughout the whole body. Mayo states that the total amount of thyroxin in the tissues of the body of a normal person is in all probability 13 mg. Each increase of 0.033 mg. (approximate) of the thyroxin in the tissues of the body, increases the rate of energy output 1 per cent. Other facts being constant, the total energy output of the body varies with the amount of thyroxin in the tissues and the rate of excitation. Plummer states that hypertrophy of the thyroid gland is an indication that the thyroid is overstimulated and is supplying the body with too much of this hormone. Colloid deposits in the gland show that it is hard worked to make enough hormone, and that is normal or subnormal. An increased thyroid action, therefore, indicates increased metabolism. According to the severity of the hyperthyroid process, this metabolism may be increased 25 per cent, 50 per cent, or even 100 per cent above normal. The heart need not be stimulated through the nervous system for its increased rapidity of action; the increased metabolism, synonymous with a call for increased energy, is sufficient to explain the tachycardia.

Function of the Thyroid

Kendall (Jour. A. M. A., 1916, LXVI) called attention to the hypotheses of Plummer, viz.: 1. In thyroid disturbances the effects are due to a change in the rate of normal function. 2. The stimulating effect of increased thyroid activity is not felt in any particular set of organs or tissues alone, but the stimulus is active throughout the body. 3. The stimulating action is intracellular. Kendall then suggests the possible formula, di-iodo-di-hydroxy-indol for the crystalline substance obtained from thyroid gland and possessing the physiologic activity attributed to the gland. He here suggests, as the result of his studies, that the function of the parathyroid is to convert ammonium carbonate into urea, and states that we may conclude that the function of the thyroid is to furnish a catalyzer which regulates the rate of deamination.

In commenting upon this subject, an editorial in "Endocrinology" notes: "The function of the thyroid, then, appears to be chiefly that of extracting and storing the physiologically active iodine, rather than elaborating an active hormone itself. That the tissues of animals are capable of utilizing iodine directly without the mediation of the gland, is shown by the results of feeding iodine to thyroidless larvæ. * * All the active substances so far extracted from thyroid tissue contain iodine; the more active they are the more iodine they contain. This is clearly shown by Kendall's Alpha substance. * * * The same principle holds true of goiters. The higher the iodine content of such glands, the greater their physiologic activity when fed to lower animals. * * The fact that iodine is capable of functioning within the organism without the gland tissue, should prove of interest to clinicians because of its bearing upon iodine therapy in the treatment of toxic goiter."

It would be presumptuous on the part of any observer to attempt a detailed description of the functions of the thyroid gland; many years of further laboratory and clinical data are still required before anyone could approach this subject with anything like absolute confidence. To briefly summarize the *existing* knowledge (such as it is) of the physiology of this organ, we may say that the most important functions of the thyroid gland are those concerned with (I) metabolism, (II) detoxication, (III) circulation, (IV) sexual structure and function, (V) intraglandular equilibrium; and I would suggest that the organ acts in the capacity of (VI) emotional mentor.

I. Metabolism

As a regulator of metabolism in the constructive and destructive phases, the rôle of the thyroid gland is amply illustrated in diseases in which there is an absence or diminution of thyroid substance, and on the other hand, where there is an increased amount of thyroid secretion circulating in the blood.

Congenital absence of the thyroid gland is the cause of cretinism, the chief features of which are perpetual infancy of body and mind. The body never attains maturity of growth; the neck is thick, the face large, lips thick, tongue bulky, skin dry and puffy, hair coarse and scanty, the limbs short, the abdomen prominent. The mental processes do not develop beyond the point of idiocy. There is mental torpor, a diminution of cutaneous sensibility and reflexes, lack of osseous, tendinous and muscular tonus, so that these patients sleep most of the time, movements are slow, bones are undeveloped, umbilical and other hernias are common, feces and urine are not properly retained, and the temperature is subnormal.

Acquired deficiency or absence of thyroid secretion (myxedema or cachexia strumipriva) as occurs after total thyroidectomy or following disease, partakes largely of the above characteristics, and may be considered as a state of adult cretinism. There is a gradual failing of the mental processes; slow, monotonous speech; poor memory; irritability; melancholia; hallucinations; and drowsiness. Tetany is an occasional accompaniment. Movement is slow and uncertain; reflexes are weak. The subcutaneous tissues become infiltrated with a mucinous substance, causing the skin to become swollen; this swelling is firm and does not pit on pressure; there is no perspiration, the skin becoming dry, rough and scaly, and assuming a yellowishwhite tint. The hair is dry, scanty, and brittle, including eyelashes and eyebrows; the nails are striated and easily broken. The features are quite characteristic, the face becoming coarse and broad, the lips thick, nostrils dilated, mouth large, and the tongue heavy. Here also the temperature is commonly subnormal. Albuminuria is the rule, and occasionally casts may be found. There is also constipation. Slow heart is characteristic. The elimination of disintegrated material is here hindered and incomplete, and a large quantity of it is deposited in and about the various cells of the body, especially beneath the skin.

It is seen that in the presence of a deficiency or absence of thyroid hormones, the metabolic balance of every cell in the body is disturbed; broken-down cell material is retained in the form of an infiltration of mucinous subcutaneous deposits; there is a cessation of growth and individuality. The subject is a helpless sloth, incapable of concentrated effort, sleeping his time away. No cell in the body of a patient deficient in thyroid secretion can be normal in structure and function. There is a hindrance of metabolic processes, which not only deters the individual's growth of body and mind, but retards also the heat-producing forces which depend upon proper oxidization of the tissues.

That cretinism and myxedema are conditions largely responsive to thyroid therapy has been known for many years. The quickening effect on growth and metabolism of thyroid substance has been conclusively shown by Gudernatsch in his experiments on tadpoles. He observed that tadpoles whose normal metamorphosis into frogs occupied from three to six months completed the metamorphosis in five to ten days when small quantities of thyroid substance were added one or more times to the living water of the tadpoles. Thus early differentiation into frogs was induced, including all the gross changes normally distributed over several months. "The miniature frogs so produced, although apparently anatomically perfect, were unstable and regularly died after a few days" (McCord and Marinus).

Many others, including the writer, have confirmed this experiment.

In Kendalls' thyroxin we have a substance capable of being employed with definiteness and precision of dosage in hypothyroidism. To quote this observer (Endocrinology, Vol. 2, No. 2, 1918): "When thyroxin is given to a myxedematous patient all the symptoms due to myxedema are promptly relieved. When it is given in too large amounts hyperthyroid symptoms are produced. * * * On these grounds it has been stated that thyroxin is the active constituent of the thyroid. * * * The moment we know that in a myxedematous patient the administration of 10 mg. of thyroxin increases the basal metabolic rate 30 per cent, we have the key to the explanation of the relief of a very complex clinical syndrome. The edema is relieved. The sluggish mentality is relieved. The dry, scaly skin becomes moist. The hair ceases to fall out and becomes soft. The voice that has been very slow, returns to its normal tone and character. The mentality which has been befogged becomes clear, and the individual expresses his normal personality. In short, every cell in the body responds with its own expression of activity. It seems impossible that all this can be done with a single crystalline substance, and because our knowledge has been limited as to just what and how much has been going on, we have let visible changes lead away into theories that are narrow and which obscure rather than enlighten. But, when we know that simultaneously with the clinical improvement the basal metabolic rate has been increased 30 per cent, it follows axiomatically, from laws of mechanics, hydraulics, and physics, that very fundamental changes have occurred throughout the entire body. It has long been known that the thyroid influences basal metabolic rate in the body. It is a present-day conception that it is through metabolic processes that the thyroid produces its physiologic effect, but the scope of this action and the chemical processes involved have not been emphasized

LANE LIBRARY

or established. * * * Plummer states that the active constituent of the thyroid determines the rate at which any particular cell can produce energy, that is, it establishes the quantum of energy which any cell can produce when it is stimulated either from within itself or from without, so that the thyroid is directly related to the production of energy within the body. He has shown that one-third of one mg. of the active constituent of the thyroid increases the basal metabolic rate one per cent in an adult weighing approximately 150 pounds. Here we have not only a definition of the function of the thyroid, but it is expressed in mathematical terms with such exactness that the number of milligrams of the substance functioning within the entire body can be estimated. It is between 23 and 50 mg., that is, between one-third and two-thirds of one grain. * * * Patients with complete atrophy of the thyroid have basal metabolic rates approximately 40 per cent below normal. It has been shown that administration of thyroxin alone can bring back and maintain the normal metabolic rate in such patients; but in complete atrophy of the thyroid, the complete or nearly complete absence of thyroxin may be assumed. The question arises as to what maintains energy output from 100 per cent below normal, which would be death, up to 40 per cent below normal, the point to which basal metabolism sinks in the absence of thyroxin. May it not be the other chemical substances in the body possessing the same grouping that occurs in thyroxin? These are amino-acids and proteins, creatin and creatinin, and a few other less well-known compounds. It seems probable that on the administration of thyroxin a reaction which has been carried on within the body by other compounds is merely increased in rate, but that there is no difference or disturbance of the reactions that have been going on."

A hyperactivity of the thyroid gland (hyperthyroidism or Graves' disease) in which an excess of thyroid secretion is thrown into the blood, is characterized by just the reverse of the above mentioned features. Every cell in the body is quickened in structural changes and in function. The mentality is hyperacute; the reflexes hypersensitive; there is insomnia; the eyes bulge forward in an ever-alert attitude; the skin is soft, thin, moist and erythematous; there is a progressive loss in weight; there is a tremor of the outstretched fingers and toes, and in fact an increased tonicity of all the muscular fibers of the body; tachycardia; often a persistent rise in temperature; chronic diarrhea; and frequent glycosuria. Here the destructive phase of metabolism is so marked that even a much greater intake of food is incapable of maintaining the body weight and strength. J. H. Means and J. C. Aub made studies of the basal metabolism of a large number of cases of exophthalmic goiter in various stages of intoxication. They found that the basal metabolism provided a very accurate measure of the degree of toxicity in these cases, being on the average within the normal limits of variation in the nontoxic cases, 43 per cent above normal in the mildly, 53 per cent above in the moderately, and 76 per cent above in the severely toxic cases of goiter.

Incidentally it may be deduced that not only should thyroid never be given in hyperthyroidism, but for obvious reasons it is strongly contraindicated in tuberculosis and other wasting diseases. An excess of thyroid substance, by engendering a state of hyperoxidation of the tissue cells, renders a patient subject to a perpetual rise in temperature, and every sign and symptom mentioned in relation to cretinism and myxedema is reversed.

E. F. Du Bois studied the metabolism in exophthalmic goiter in a respiration apparatus which is also a calorimeter. Thirty-six observations were made on 11 patients with this disease, and six experiments were made on a cretin. The heat production was an index of the severity of the disease and the effect of the treatment. There was an increase of 75 per cent in very severe cases, 50 per cent in moderate cases, while in mild cases it may be within normal limits. The tachycardia, cardiac enlargement, and emaciation quite probably are due to increased metabolism. The increase in average water elimination through the skin and lungs is closely proportioned to the increase in heat production. Rest in bed caused a material fall in heat production. This is the only form of conservative treatment that appeared to cause a reduction in metabolism. A cretin, thirty-six years old, produced half the calories eliminated by children his size. His metabolism was 20 per cent below the normal adult level, estimated by the skin surface area. Three and a half days of treatment with thyroid extract raised his heat production to normal (Endocrinology, Vol. I, 1917.)

We have pointed out that the metabolic functions of the thyroid gland embrace a maintenance of the proper mental and physical stability, growth, and bodily heat, all these through the maintenance of a balance between the constructive and destructive forces of cellular life. To exemplify further, it has been found that delayed union in fractures is sometimes due to deficient thyroid substance, for the administration of thyroid gland has yielded excellent results in some instances. The same has been said of some cases of chronic articular rheumatism: Paul Claisse has obtained good results in several instances of the degenerative type of chronic rheumatism with the use of desiccated thyroids. The painful, slow movements in some cases of supposed myalgia or muscular rheumatism are due to the mucinous infiltration within the muscular tissues consequent upon a degree of hypothyroidism, frequently resulting in cure by the administration of thyroid and the iodides. A similar infiltration along the nerve sheaths and tissues giving rise to evidences of neuritis, likewise yields to this treatment. The central nervous system is not immune to this infiltration process of thyroid deficiency; J. Madison Taylor has employed thyroid gland successfully in the treatment of persistent somnolence; very gratifying results have been obtained by the use of thyroid extract in various forms of mental aberration, such as melancholia, mania, hypochondriasis, and hysteria. Vertigo, dizziness, and mental confusion frequently yield to the same treatment. The skin is markedly influenced by the thyroid secretion; in diminution or absence of the latter, the skin becomes dry, thick, and scaly; in the presence of an excess, the skin is exceedingly moist and thin. Thyroid administration promptly overcomes the skin manifestation in the hypothyroid state and often relieves also the various skin diseases associated therewith; dermatologists everywhere have recognized the wonderful therapeutic virtues of thyroid in some instances of scaly eczema, psoriasis, ichthyosis, pruritus, alopecia, and other forms of skin affections presumably due to thyroid deficiency. Even the teeth suffer from a lack of this vital secretion. Under the heading of "Thyrodontia," D. M. Kaplan (Endocrinology, Vol. I, 1917), in a valuable paper on this topic, remarks: "It is a fairly well-established fact that the calcium metabolism is governed chiefly by the thyroid apparatus, and secondarily, by the rest of the endocrines. The alkalinity of the saliva to a certain extent depends upon calcium salts. It is to be seen how a disturbed endocrine equilibrium could bring about dental decay by a disturbance in the calcium metabolism balance, particularly in children, who depend upon their thyroid and thymus more than the adult and the senile. The calcium being deficient, the acids of food decomposition are not neutralized, and the dentine consequently suffers, this being one of the stages in the complete breaking down of the tooth. In children particularly, a well-balanced thyroid and sound teeth go together. If the thyroid is not performing its duties properly, the tooth to suffer first is the molar. The submaxillary saliva is said to be richer in calcium than the parotid, and in view of the fact that the molars lie behind the duct their supply of immunizing saliva is less than the front teeth, and hence, in case of calcium deficiency, they succumb first. This is manifestly apparent in the longer life of the lower front teeth as compared with the upper, the latter not having the constant salivary bath enjoyed by the lower teeth. This is very characteristically displayed by the woman with an exhausted thyroid, due to repeated pregnancies, who invariably loses her upper incisors. Of course in such women the other endocrines enter into the mechanism conducive to the dental loss.

"To start with, thyroidal teeth are distinguished by their slender frame, they are thinner, more transparent and graceful, and their color tends toward a bluish-gray-white. Children and married women with such teeth can be saved a great deal of dental trouble by the discreet and timely administration of thyroid extract. The frequency of the therapeutic display depends entirely upon the case and the acumen of the physician.

"In the multipara the dental situation from an endocrine point of view is only partly thyroidal. The interplay and compensatory work of all of them are necessary to help her through this physiologic symbiosis, and if the woman is deficient in any of the endocrines she will display not only dental changes, but all kinds of other objective and subjective manifestations depending upon the glands or gland involved. The falling out of the upper incisors independent of decay, bears a distinct pituitary stamp, and one may say that the maxillary sockets become too large in some pregnant women, and that the root is not firmly implanted in such a jaw, at this episode of partial transient physiologic acromegaly. It is the duty of the discerning physician, as well as the dentist, to guard against irreparable loss, disfigurement and suffering of patients by a timely use of thyroid extract in cases of dental caries or late irruption, as well as in gestation that promises injury to the teeth."

To make a simple analogy, it can therefore be concluded that the effect of thyroid secretion on metabolism is somewhat similar to the relation of the fuel to a furnace. A *normal* amount of thyroid substance within the tissues keeps them in a state of poise or equanimity, *i.e.*, in an equilibrium between destructive and constructive forces whereby the individual is said to be normal in structure and function of body and mind. A *diminution* of this secretion keeps the furnace low, and we have a diminished "burning down" of material plus the lessened elimination of waste matter through the blocking of the "draught," because of lowered function of excretory organs; thus the patient's physical and mental activity is somewhere between normality and zero, depending on the degree of the affection. An *increased* quantity of thyroid secretion creates a state of extreme "firing" of the bodily furnace; the balance between anabolism and katabolism is broken in favor of a tremendous increase of oxidation of body tissues which "burn down;" during the process there is a marked quickening of all eliminative functions, with the result that the patient becomes almost a shadow of his former self.

II. Detoxication

It is the presence of iodine in the thyroid gland which seems to have given rise to the theory that the organ possesses an antitoxic, defensive and immunizing action against endogenous and exogenous poisons. On investigating the question of resistance to infection, the removal of the thyroid establishes the fact that in thyroidless animals infection is much more prevalent. The gland is looked upon, says Crookshank, as " a kind of trap or catchpit in which obnoxious material is destroyed and its elements converted to good purpose. Even so are products of waste and disintegration converted by the cells of the liver into what Glisson called 'Bile: that variously beneficial balsam of the body.' " "I am personally inclined to believe that one function of the gland may be a detoxication, but I do not believe that this is accomplished by a direct chemic union of the thyroid secretion with a metabolic toxin, but rather by the stimulating and regulating effect which is exerted on other viscera" (S. P. Beebe). It is to be observed, therefore, that this function of detoxication is accomplished by a proper interaction with the liver, pancreas, and other organs of the body.

On the other hand, the body does not seem to possess greater immunity to intoxication when iodine or its compounds are administered by mouth. Although Reid Hunt concludes from his experiments that the administration of thyroid to animals rendered them capable of resisting such poisons as acetonitrile, which neutralizing ability was approximately parallel to the iodine content in the blood, this is not so with human beings. H. R. Bassinger, dissatisfied with previous results, attempted to solve the problem by injecting minimal, subminimal and repeated subminimal lethal doses of diphtheria toxin into the thyroid of a dog. In a second series of cases he used tetanus toxin. He found that minimal lethal doses caused death more rapidly than in the control dog. Subminimal doses, that is, about one-tenth of the former, produce only the slightest symptoms of toxemia. The colloid in the glands was the same as in the controls. Repeated subminimal doses produced no hyperplasia nor increase of colloid. He concluded that the thyroid has no detoxicating properties that can be demonstrated by the injection of diphtheria or tetanus toxin into the thyroid. Microscopic examination showed no increase in colloid, repeated injections caused some resorption of colloid but no active hyperplasia. It must be said, however, that the action of the iodides upon the lesions of tertiary syphilis is really due to the action of the thyroid which is instigated by this administration. Says Rendel Short (quoted by I. G. Cobb): "I have found thyroid extract quite as effectual as iodide of potassium in healing tertiary syphilitic ulcers."

It has been frequently demonstrated that the thyroid acts as a storehouse for iodine. This has given rise to the hypothesis that the Basedow syndrome is caused by iodine which is not stored and can not be metabolized by the thyroid. In other words, according to this theory, Graves' disease is perhaps due to the failure of the thyroid gland to control iodine metabolism, and the continued intake of iodine into the system with the food, without its being metabolized, is the cause of the toxic state.

Von Cyon (quoted by Crotti) believes that the principal function of the thyroid is to transform iodine compounds into a harmless, organic combination, the *iodothyrin;* Blum that the thyroid neutralizes in the gland itself the toxic products of intestinal origin, the enterotoxins. Blum believes that foods poor in iodine are the most poisonous, that those containing the most iodine are nonpoisonous and nontoxic, and that the ones saturated with iodine are harmless.

H. D. Bishop and other observers conclude that the toxemia of pregnancy which expresses itself in eclampsia as its climax is due to an autointoxication from imperfect metabolism primarily caused by a failure of the organism to transform properly the waste products of the mother and fetus by the normal processes of oxidation. This in turn is believed to be the result of imperfect functional activity of the thyroid and that the rational treatment of such disturbances in the metabolism is to supply the active principles of the thyroid secretion. Thyroid extract is often given not only for the treatment of eclampsia but as a prophylactic, to aid in the proper metabolic functions of the secretory and excretory organs, to assist the processes of nutrition, enhance the metabolism of nitrogenous materials and the elimination of poisonous products, especially from the kidneys and liver.

III. Circulation

The influence of thyroid substance on the circulation is almost startling when illustrated by the effects observed following the administration of overdoses of thyroid extract. The heart action is markedly accelerated to twice its normal rate; there is a lowering in blood pressure; and if this action is long continued, the pulse may become irregular. Vasodilator effect of the thyroid is seen when administered in eclampsia. Thyroid secretion is obviously contraindicated in organic or functional heart disease. Whether the effect of thyroid on blood pressure is due to a depression in the function of the pneumogastric nerve, the stimulation of the acceleratory fibers of the sympathetic, or both, is still a matter of conjecture. There is no doubt that the thyroid, by its interrelation with the pituitary body and the adrenals, serves to govern and regulate the heart's action, the vascular tone, and the blood pressure. In deficient thyroid secretion, bradycardia is common; the heart's rate is often as low as 40 per minute.

The blood vessels evince a degree of vasomotor instability in the presence of hyperthyroidism, as seen in the irregular areas of erythema and the dermographia of the Basedowian patient, and the increased action of the sweat glands, due to an increased blood supply to their acini. In hypothyroidism the skin is waxy in hue, dry, scaly, and puffy, frequently presenting areas of disease.

The blood in the presence of excessive doses of thyroid substance becomes disintegrated, coagulability is delayed, and there is often a state of hemophilia supervening. Occasional instances of persistent menorrhagia, attributed to a deficiency of thyroid secretion, are favorably influenced by the administration of thyroid extract.

Even the lymphatic system seems influenced by an increased quantity of thyroid secretion; the thymus is commonly enlarged, and there is often an associated generalized enlargement of the other lymphatic glands of the body.

IV. Sexual Development

That the thyroid gland and its secretion influence the growth and functions of the sexual organs is thoroughly established. "The connection between the thyroid and the sex organs is intimate. It is well known that the men in India can tell in a moment whether their women have been tampered with by the condition of their thyroid"(Lane). Delay in sexual development and growth is often given an impetus when thyroid is administered. In the higher invertebrates the thyroid is intimately related to the sexual functions, and in man this relation is inseparable. D. Marine states that there is evidence in man of thyroid sex gland interrelation recognizable not only in the female in association with the development of secondary sexual characters, with menstruation and pregnancy, but also in the male at puberty, though to a very slight degree. The meager evidence available would tend to indicate that the interstitial cells of the ovary, and perhaps also the adrenal cortex, play a major rôle in this relation in the female, as certainly the cells of Leydig do in the male.

It is generally conceded that the thyroid is larger in women than in men, and it is relatively larger in children than in adults. Huschke and Krause assert that, while in the newborn child it is in proportion to the weight of the body 1 to 400 or even 1 to 420, in the adult it is 1 to 1800. (Havelock Ellis). In old age the gland is relatively diminished in size and is not likely to be followed by as serious results when extirpation is performed, as would be the case in the prime of life. "The thyroid gland plays a very considerable part in the characteristics of the two sexes. The female is sharper witted, more voluble, and less stable. A woman often jumps to a conclusion without any process of reasoning, but simply by intuition gets there and sticks there, and no line of reasoning will convince her that she is not right. Thyroid metabolism has much to do with this process; women of the more reasoning type have their suprarenals perhaps more developed than their thyroids, and present other masculine characteristics" (Beebe and Beveridge).

Havelock Ellis, in his book "Man and Woman," presents some interesting facts regarding the relationship of the thyroid gland to woman's sexual life. He asserts, as indeed has been hinted by many others, that the gland follows closely all the variations in a woman's organism to so marked an extent that Meckel long ago remarked that the thyroid is a repetition of the uterus in the neck. The fact that the neck swells in women in harmony with the sexual organs seems to have been an observation made in very early times. Aside from the observed swelling of the neck during menstruation, pregnancy, and disorders of the uterus and adnexa, increase in the circumference of the neck has been considered an accompaniment of the first sexual intercourse, and it is a very ancient custom, says Ellis, to measure the neck of newly married women in order to ascertain their virginity, which custom still prevails in the south of France. Heidenreich, quoted by Ellis, found that a similar swelling occurs in men at the commencement of sexual relations. Herman Freud finds congestion of the thyroid in 45 out of 50 cases of pregnancy; furthermore, it increases in volume at the birth of the child, and occasionally continues in this state during lactation.

Diseases of the thyroid are most common in women, and simple goiter occurs, according to opinions of various observers, in different localities, in from one man to two women, to one man to fifteen women, though cretinism is more common in males. Myxedema, on the other hand, is most common in middle-aged women. Exophthalmic goiter is most common in women, but this preponderance is not as great as some would have us believe. In my experience, I find the proportion approximately two men to three women.

Puberty is accompanied by an increase in the thyroid substance in both sexes, and is merely compensatory to the demands of the growing developing organs for more thyroid secretion. In the female, this enlargement is more marked, often approaching in size an appearance of goiter.

During menstruation, the thyroid is larger than before, and it is at that time that mental disturbances are apt to arise in the absence of physical and mental rest.

During pregnancy, not only is the thyroid unduly full, but a typical goitrous growth not infrequently occurs. The organ may or may not become normal in size after parturition, and if some of the hyperplasia becomes permanent, subsequent pregnancies, by repeating the process, often lead to the development of a typical goiter. A certain degree of hyperactivity of the gland is probably the natural safeguard against the toxemia of pregnancy, so that thyroid gland is frequently given by some clinicians with this purpose in view, both as a prophylactic and as a curative agent. In this connection, it may be remarked that the irritable, whimsical pregnant woman so often encountered by obstetricians, to say nothing of occasional instances of puerperal psychosis, is thought to be a form of thyroid toxemia not unlike that of hyperthyroidism, and it is often advisable to treat such cases along these lines.

The functions of the thyroid gland do not omit supervision over lactation. Not only is the thyroid persistently enlarged during this period, but it has been found that where the milk is not forthcoming in sufficient quantities, the administration of thyroid extract seems as an impetus to its secretion.

The menopause is often profoundly influenced by the thyroid gland, and many of its symptoms are apparently due to an alternating hypo- and hyperactivity of the organ.

Many of the diseases of the uterus and adnexa are intimately associated with thyroid function. In thyroid insufficiency, the pelvic organs remain small and infantile; menstruation occurs rather late in life and is irregular and often characterized by menorrhagia. Salzman believes that certain uterine hemorrhages are the result of an alteration or lack of one or more of the hormones which control the normal uterine flow. He believes that uterine hemorrhage in which there is no discernible pelvic disease or pathology, and in which there is no evidence of the so-called "hemorrhagic states," is due to a deficiency in the secretion of the thyroid gland. Accordingly, such a hemorrhage should be controllable by the judicious exhibition of thyroid gland. This author reports six cases of hemorrhage of this character which substantiate his opinion. Because of the intimate physiologic relationship of the thyroid and the gonads, von Fellenburg administered thyroid extract in a number of cases of sterility with no apparent cause. Conception followed in several of the cases. Those to whom this treatment is given should be kept under close observation, the heart being watched and the blood counts made from time to time. Habitual abortion is believed by some to be due in a large percentage of cases to a deficiency in the thyroid hormone; especially is this the case in the presence of obesity. The administration of thyroid extract frequently results in cure and childbirth. Dysmenorrhea, endometritis, subinvolution, and other affections of the uterus and adnexa frequently yield to thyroid therapy. W. H. Veil describes two cases of women with normal sexual function in whom a strumectomy was performed. In both cases too much of the gland was taken away, and the symptoms of myxedema developed. The menstruation became irregular, both women showed all symptoms of a true menopause: the uterus became smaller, and at last menstruation ceased. In both cases a perfect recovery was observed after administration of thyroid gland.

V. Interglandular Equilibrium

That the thyroid gland is strongly concerned with the maintenance of the functional balance between the endocrine and other organs of the body, is attested by the accumulating evidences of physiologists throughout the world. Kendall (Journal-Lancet, 1917, 37) thus sums up the relation of the thyroid to the other ductless glands in the bodily cellular changes: "While it has not been proved beyond controversy, there is much evidence to support the hypothesis that the function of the thyroid is to furnish the animal organism with ammonia resulting from the diaminization of amino-acids. The amino-group in amino-acids is unavailable for the formation of urea and other nitrogenous compounds until it has been split out of the amino-acid. This diaminization seems to be the function of the thyroid.

"The thyroid hormone is involved in the first split of ammonia from the amino-acids. The adrenal cortex secretion then converts this substance into some other, and the secretions of the thymus, the parathyroids, and other glands are involved in the further elaboration of the nitrogenous constituents which finally appear in the urine. It is therefore evident that the administration of the thyroid hormone merely starts an increased rate of production of ammonia, which, in itself, does not produce hyperthyroid symptoms. It is only when the other ductless glands are stimulated that the reaction is carried on at a rate sufficient to change the basal metabolism, the irritability of the nerves, and the other effects produced by administration of the thyroid hormone. These reactions take place within the tissues and, in part, within the blood; and the speed with which they occur, and hence the equilibrium maintained, producing an increase or decrease in metabolism, depend on the stimulation of the various endocrine glands and the ability of the tissues to carry on the reactions which are made possible by the secretion from the various glands."

The relation of the thyroid to the *parathyroids* is intimate, not only because a rapid enlargement of the thyroid gland may, by pressure upon the parathyroids, bring about symptoms of parathyroid disease, but also because the functions of the two are closely interrelated. In cretinism and myxedema symptoms are often observed which are directly traceable to parathyroid insufficiency. Moreover, it has been noted that tetany is improved by thyroid administration. It has also been seen that the administration of parathyroid substance, especially combined with calcium, is effectual in overcoming the tremor of hyperthyroidism. For these reasons, Gley believes that the parathyroids are part of the thyroid gland, being an embryonic and partly developed tissue.

The thyroid function is related to the *pituitary* in that the latter is seen to undergo extensive increase in size in thyroid disease, especially cretinism and myxedema, indicating an attempt at compensation for altered thyroid function. The administration of pituitary extract in exophthalmic goiter has yielded success in the hands of S. Solis-Cohen and other able clinicians.

The function of the thyroid includes a relationship with the *suprarenal* glands, and in the presence of a change in function of one, the others are affected. This is amply illustrated not only by the influence exerted by the results of the administration of extract of suprarenal gland in cases of hyperthyroidism, but also by the presence in the clinical picture of Graves' disease of areas of pigmentation not unlike those seen in Addison's disease. Indeed, occasional instances have arisen where, in the presence of universally distributed pigmentation of the skin and mucous membranes, it is difficult to differentiate between Graves' disease and Addison's disease. The intimacy of interaction between the thyroid function and that of the suprarenals is more specifically emphasized by the following observations:

Ott and Scott have reported that intravenous injections of thyroid extracts increase the adrenin in the blood of animals, but they obtained the same results with extracts of other organs. Hoskins, just prior to this, showed that the administration of thyroid substance to newborn guinea pigs produced hypertrophy of the adrenals. Pregnant adult pigs, similarly fed, however, gave birth to young in which the average weight of the adrenals was below normal. These apparently paradoxical observations were explained by the suggestion that the blood of the mother, overladen with the adrenal hormones, had inhibited the growth of the fetal adrenals. Herring later showed that the administration of raw ox thyroid in large doses to cats, increases the amount of adrenin in the adrenals. The weight of the adrenals was found to be increased. This observer later showed that the administration of small doses of thyroid gland to white rats produces hypertrophy of the cortex and medulla of the glands, with increase of the adrenin content. The hypertrophy of the cortex was found to be somewhat greater than that of the medulla. Accessory suprarenal tissues were also found to undergo enlargement. Goetsch observes that in cases of Basedow's disease, the intradermal reaction to minute doses of adrenin is exaggerated. He also observed that subcutaneous injections of adrenin in these cases greatly increase the symptoms. These reactions, he states, vary directly with the intensity of the symptoms or, as most authors believe, with the amount of thyroidemia. Cannon and Cattell have shown that injections of small doses of adrenin produce an action current in the thyroid and hence secretory activity in the gland. Stimulation of the splanchnics, leading to adrenal discharge, produces the same results. Levy observed that the injection of adrenin sensitized the motor system to the action of succeeding injections of adrenin. He brings forth evidence to show that this sensitization is due to thyroid discharge produced by the first injection of adrenin. In summarizing this phase of the subject an editorial (Endocrinology, Vol. I, No. 3, 1917) remarks: "The weight of existing experimental and clinical evidence supports the theories that the thyroadrenal interrelation is one of mutual stimulation; that the thyroid secretion sensitizes sympathetically innervated tissues to the action of adrenin, and that they both act on the sugar deposits in the body, producing a liberation of carbohydrates."

The influence of thyroid function on the various phases of *sexual* life and the structure and function of the sexual glands has already been mentioned. It may be reiterated that a deficiency of thyroid secretion is accompanied by a marked diminution in growth and function of the sexual makeup. Removal of disease of the ovaries or testicles is frequently followed by enlargement of the thyroid.

The interrelationship of the thyroid with the *thymus* gland has given rise to volumes of speculation, in that a large number of patients with a hyperactive thyroid seem to possess a coexisting hyperplasia of the thymus gland. Some observers have ventured to state that the thyroid tends to stimulate the growth of the thymus. In this connection a thought frequently arises in my mind: Is this increase in size of the thymus in hyperthyroidism a mere coincidence, or is there some sort of casual relationship one way or the other? It seems to me that the latter conclusion will remain untenable until it can be proved that the same percentage of normal persons does not present an abnormally large thymus gland.

"'Hyperactivity' of the thymus is frequently described where percussion indicates a dullness in the region of the sternum or a shadow is shown there by X-ray. This condition is described in cases of 'mors thymica' and exophthalmic goiter. As a matter of fact it is questionable without an autopsy whether such enlargement of the thymus is not due simply to an unusually large deposit of fat. Often the size of the thymus is maintained in this manner, although relatively little thymic tissue is present. Moreover, the variability of the thymus is so great that the gland often persists normally until late in life, as is disclosed by autopsies of accident cases. Anatomists make an allowance of from 100 to 700 per cent in the normal weight of the thymus at different ages * * * Melchior has pointed out the fact often disregarded, that although an 'enlarged' thymus is frequently found in exophthalmic goiter, the symptoms are not different when the thymus is not enlarged. * * A more logical theory of the significance of the thymus is that its functions as a lymphoid organ in infancy and childhood when large numbers of lymphoid cells and leucocytes are needed to combat infections. The large number of leucocytes and especially lymphocytes in the blood during this period of life indicates that these cells are relatively very important to the organism. The question of the relative loss of thymic tissue and other lymphoid tissue all over the body that begins at birth and progresses throughout life, especially in infancy and childhood, must be bound up with the question of the development of immunity from, or resistance to, infections that occur in every animal. It is a fundamental law of biology that bodily structures the need for which decreases, tend themselves to atrophy" (E. R. Hoskins).

Sajous states that the interaction of the thyroid with the thymus through the agency of the lymphocytes of the latter, probably regulates the supply of excess of phosphorus in organic combination which certain systems, particularly the osseous and the nervous, required during development and growth. The same may be said of the other lymphatic glands of the body which are frequently found enlarged in hyperthyroidism.

Investigations have proved that the functions of the thyroid gland and those of the *pancreas* are somewhat antagonistic. M. Kojima has shown that after a week of thyroid feeding the pancreas of the rat shows typical changes; the alveoli are smaller, the alveolar cells are smaller, the nuclei vary in size and staining capacity, the cytoplasm of the cells contains comparatively little zymogen, and there are many mitotic figures, indicating rapid multiplication. After an intermission in the thyroid feeding these changes disappear. The thyroid gland exerts an inhibitory action upon the pancreas, and vice versa. Extirpation of the thyroid gland renders the pancreas hyperactive, and contrariwise, an increased function of the thyroid gland depresses pancreatic function as evidenced by the common occurrence of glycosuria in Graves' disease and by the fact that in myxedema large quantities of sugar may be ingested without producing glycosuria. In this connection it is of interest to note the remarks on the work of Janney and Isaacson: "Previous work in some cases has shown a decrease in blood sugar and in some an increase when the thyroids are removed. Injury to the parathyroids is probably one factor in the disparity. In Janney's and Isaacson's dogs at least two parathyroids were left intact and the freedom of the animals from tetany showed that functional integrity had been maintained. After the thyroidectomy the blood sugar averaged about 25 per cent lower than normal. Glucose feeding resulted in less elevation of the blood sugar level after than before thyroidectomy. On the grounds that cretinism, myxedema, Addison's disease and experimental adrenal deficiency are all marked by hypoglycemia, the authors offer this as a general sign of endocrine deficiency. They suggest that diabetes mellitus might possibly be benefited by removal of thyroid tissue" (Endocrinology, Vol. I, 1917). Thyroid substance is obviously contraindicated in the obesity of diabetes.

The influence of thyroid function upon that of the *liver* has occupied the minds of many experimenters; it has been concluded that the storage of glycogen and its discharge from the liver is regulated. Kuriyama has shown that the administration of 3 to 5 gms. of desiccated thyroid of pigs administered to white rats, decreased the glycogen content of the liver in three to five days, and proved that the influence of thyroid feeding on liver glycogen can be removed by omitting thyroid from the diet. Cramer and McCall conclude that the thyroid secretion produces an increased oxidation of carbohydrates. The action is not direct, but "follows its action in discharging glycogen from the liver." They distinguish an "early" stage (second or third day after feeding thyroid) and a "later" stage (third to sixth day). In the "early" stage the preexisting carbohydrate of the food and of the deposits in the organism is oxidized. In the "later" stage there is, in addition, a formation of carbohydrates from protein and possibly also from fat, and a subsequent oxidation of carbohydrates thus formed. There is a marked rise in carbon dioxide excretion and oxygen absorption. These observers state that the action of the thyroid secretion on the glycogenic function of the liver lies thus at the root of the increased oxidation of the proteins, carbohydrates and probably fats produced by thyroid feeding. Experimental hyperthyroidism does not change the sugar content of the blood in rats or rabbits. Neither does spontaneous glycosuria occur from thyroid feeding in these animals.

The thyroid stimulates the *kidney* secretion, exerting a diuretic influence. This has been amply illustrated in many instances of nephritis of the parenchymatous type in which thyroid gland was administered with resulting increased output of urine and diminution or disappearance of albumin and casts. C. Phipps reports the use of thyroid in numerous cases of nephritis with, on the whole, beneficial results. One patient could not tolerate it and in one case it had to be omitted from time to time on account of its apparent toxic effect on his heart. The other cases showed rapid improvement of the edema and relief from uremic intoxication when present. None of these cases died. The same effect is seen when thyroid is given in eclampsia. In cretinism and myxedema, the output of urine is diminished, and albumin and casts are common.

Even the *gastrointestinal* secretions are stimulated through the thyroid gland. In hyperthyroidism we have an increased secretion of the intestinal mucosa with consequent diarrhea. Contrariwise, the diminished secretions of the intestines in hypothyroidism engender persistent constipation, autointoxication, and tympanitis.

VI. Emotional Mentor

The thyroid has for a long time been called by the French *la glande de l'émotion,* because of the observed phenomena during aberrations from one's mental poise, and because of the frequency with which exophthalmic goiter is seen to follow shock to the emotions. In an individual suddenly aroused to fury or anxiety, or confronted with a fearful situation in which the instinct of self-preservation is the permeating or governing factor, the heart thumps away at a tremendous rate, the breathing is hurried and shallow, the skin becomes cold and clammy, beads of perspiration stand out on the forehead, the eyes stare ahead out of their sockets, the whole frame trembles, there is often an irrepressible desire for the expulsion of rectal and bladder contents, and the individual feels a choking sensation in the neck, stating that "his heart is in his mouth," and causing him to insert his fingers between the neck and collar in order to stretch the latter to facilitate breathing. An analysis of this state will prove it to be a typical case of exophthalmic goiter in a transient form. There is a temporary tachycardia and palpitation, diminished respiratory expansion and dyspnea, hyperidrosis, exophthalmos, tremor, tendency to diarrhea and polyuria, and fullness of the thyroid. The term "chronic fright" as applied to exophthlamic goiter is highly applicable and indicates very tersely almost the entire symptomatology of the disease.

No emotion is free from a concomitant physiologic hyperactivity of the thyroid gland. Even joy, laughter, hilarity, and ecstasy are accompanied by an increased thyroid vascularity and function. The event of the first connubial experience, so often mentioned by the older writers as associated with thyroid enlargement, is not a state merely of organic interaction or glandular interrelationship, but here also the sexual emotions play a prominent causative part.

What is the function of the thyroid during the emotions? As this phase of the question of thyroid physiology has not been seriously studied, we can only make casual speculations and deductions. The features of a cretin or of a subject of myxedema are stupid and expressionless. In the event of the "figuring out" of a given situation in which quick thinking and acting are vital (*i.e.*, in case of a conflagration, a runaway, shipwreck, or an attack by a highwayman), there is little if anything "doing in the upper story," to use a slang expression. Without the thyroid, there is no cerebration, no normal adjustment between internal and external relations. The instinct of self-preservation has not that strong, impulsive, impetuous physical backing,—that storm or drive of fight or flight common to the normal creature.

In the average being, an emergency situation is met quickly and usually with reasoning (depending upon the individual's previous experiences and mental training) often better than if there were an opportunity for premeditation. The thyroid sends out its surplus of hormone, stimulating the brain cells and whipping up the circulation, so that every cell in the economy is quickly supplied with the necessary armament to back up the self-preserving instinct. If the subject takes flight, the decision is almost instantaneous, and he runs better and with more vim and strength than ever before, and only complete physical exhaustion can stop him. If he fights, he does so even against great odds, not at all heeding the terrific punishment he receives. If it is necessary to jump from a burning building, it is done promptly and to a place of safety, if there be one. And if the situation requires jumping overboard from a shipwreck, he does so without hesitation and often swims to safety, even though he never swam before.

Occasionally, a person with an hereditary tendency or individual idiosyncrasy will, instead of acting quickly in self protection, become momentarily paralyzed as it were. He has plenty of thyroid, but there is a sudden blocking of the mental and physical "drive" common to normal persons, and he is helpless. It is from this class of reactionless individuals, persons in whom the thyroid worked tremendously to bring results but without avail, the organ being incapable of recoiling back again to the normal, physiological balance, that we have our cases of Graves' disease.

Conclusions

In the present stage of our inquiries into the rôle of the thyroid gland in health and disease, one is impressed by the apparent universal influence the gland exerts over the vital processes of animal life. Not a cell in the body, no matter how simple or specialized, but what its integrity is directly or indirectly supervised by the thyroid; not an organ but what its structure and function are influenced by an increased or diminished activity of the thyroid. Even the elements of the blood, the secretions and excretions of the body, are directly or indirectly altered in quality and quantity by the "whims and fancies" of the thyroid gland. On the other hand, clinicians and endocrinologists are becoming convinced that disturbances elsewhere, *i.e.*, diseases of sexual organs, liver, pancreas, respiratory system (especially a diseased condition of the nose, throat, and mouth), gastrointestinal tract (autointoxication, chronic appendicitis, etc.), the other endocrine organs and the nervous system (especially through emotional shock), may so influence thyroid structure and function as to engender a picture of Graves' disease.

As clinicians, what practical deductions may we draw from our knowledge of thyroid function to assist us in the successful management of a case of exophthalmic goiter?

1. "The thyroidal functions are complex, and the secretion polyvalent; hyperthyroidism or Graves' disease may be provoked by agencies as varied as the functions of the organs; progression in a vicious circle happens most readily to those who, by constitution or by acquisition, possess a particular type of nervous or endocrine balance" (Crookshank).

2. Hyperthyroidism is not due to changes in structure and function of the thyroid gland alone; disturbances in this organ constitute but one link in the chain of events indicating a *pluriglandular* disorder—a widespread disturbance of intra- and interglandular equilibrium.

3. Since Graves' disease is pathologically and clinically not a local condition, local treatment, especially local surgical interference, is an illogical procedure.

CHAPTER III

PATHOLOGY OF EXOPHTHALMIC GOITER

Because of the universal changes occurring as a result of the increased metabolism in this disease, hardly any organ escapes injury. But since the affection is due to the presence of an excess of thyroid substance within the bodily fluids and tissues, and since it is the thyroid gland which elaborates this substance, we are concerned especially with the consideration of the pathology of this organ.

The Thyroid

The cardinal pathologic status here is hyperplasia, with or without enlargement of the gland. Macroscopic increase in size of the thyroid, though usually present, is not invariable, nor does the severity of the symptoms bear any relationship to the size of the gland. Kocher and others have found hundreds of cases in which physical examination revealed no enlargement. Not only are some thyroids normal or even smaller in size in the presence of a severe Basedowian syndrome, but it has been shown that in these cases the hyperplastic condition is marked. McCarrison states that in Murray's series of cases goiter was absent in 4.3 per cent. In my experience, in the cases not presenting goiter (approximately 5 per cent), there is usually a thickening of the right lobe which is difficult to distinguish from the anterior border of the sternocleidomastoid muscle, but which moves up and down with deglutition and is tender to deep palpation. It must be recalled that in the absence of goiter there is the rare possibility of a hyperplasia of an accessory thyroid.

The usual case presents a goiter of variable size sooner or later, some time after the onset of tachycardia, palpitation and nervousness. The swelling is soft and diffuse, variable in extent, and is made more prominent by having the patient hyperextend the neck. Because of its vascularity it is reduced by squeezing, the blood emptying itself out of the gland in a somewhat sponge-like fashion. Deep palpation, especially when the neck is in extension, elicits tenderness. On inspection, the gland often presents an expansile pulsation, and if the condition has existed for some time, the carotids, subclavians and other superficial vessels also pulsate. Occasionally this pulsation, especially when the heart has become hypertrophied, is so generalized that the head and even the trunk of the patient is seen to shake or vibrate with each cardiac cycle. A thrill is felt by the palpating hand over the gland, and a bruit, systolic in time, sometimes also diastolic, rather harsh and loud, is usually heard over the gland and often over the vessels of the neck. These phenomena, that is, the throbbing, compressibility, tenderness, thrill, and bruit, are rarely present in simple or nontoxic goiter, and are pathognomonic of a hyperplastic or Basedowian thyroid.

"The syndrome may exist with a normal thyroid, with a colloid goiter, a hyperplastic or atrophic goiter, or with a tumor of the thyroid" (Marine). Marine and Graham state that among the cases of exophthalmic goiter in which autopsy was performed by George W. Crile and his associates, there were seen no normal thyroids; hyperplasia was present in about 70 per cent, most of the remaining 30 per cent being adenomas with a few colloid goiters. Brissaud, in 25 cases, found changes in the thyroid, and though the lesions were neither typical nor constant, they were such as to render hypersecretion possible. Plummer is convinced that the disease is caused by thyroid hyperplasia.

The anatomic changes of true exophthalmic goiter may be led on from an active thyroid hyperplasia to a degree of degeneration, with hyposecretion. The latter explains the not infrequently occurring manifestations of hypothyroidism coexisting with or following Graves' disease as a sequel. Degenerative changes may occur rapidly or slowly, with lessening or remission of symptoms, and may result in an apparent cure of the patient. Bumstead states that the primary hyperemia of a typically developing case of Graves' disease is accompanied by an increase of interstitial and parenchymatous tissues and often an increase of alveoli which contain a thin colloid secretion.

Generally speaking, a specimen from a case of Graves' disease presents an equal enlargement of all its parts. The enlargement rarely assumes great proportions, the lateral lobes usually attaining a size somewhat smaller than a goose egg, and the isthmus correspondingly enlarged. The surface is usually smooth, but a cut section presents quite a characteristic appearance. There is seen a homogeneous structure not observable in ordinary parenchymatous goiter, with little or no visible colloid. The blood vessels also differ from those of a cut surface of parenchymatous goiter in that they are smaller and less numerous. Cases of years' duration show diffuse adenomatosis or encapsulated adenoma, or regenerations of previously atrophied parenchyma, but such cases are not true exophthalmic goiter (L. B. Wilson).

Microscopically, an exophthalmic goiter presents a moderate quantity of colloid; occasionally this is much reduced in quantity or even entirely absent. The increase in the number and shape of the cells, the increase in the number of alveoli, diminution in alveolar colloid and its contained iodine,—it is these characteristics which serve to distinguish the thyroid of exophthalmic goiter from the thyroid of simple or nontoxic goiter. Rautman states that in Graves' disease the thyroid gland seems to have reverted to an infantile type, the histologic findings resembling those of a child's thyroid. The vesicles are little, if at all, distended, and the epithelial elements have undergone a varying degree of proliferation depending upon the degree of hyperplasia of the gland, but not necessarily upon the severity of the symptoms presented. The specimen presents a picture of glandular hyperactivity, excepting that the products of secretion are diminished or absent, having passed into the circulation almost as soon as manufactured. Berry states that an extreme case presents considerable superficial resemblance to a round cell sarcoma.

Many varieties of atypical specimens are encountered. For example, an exophthalmic goiter, especially one of unusual size, may present one or more cysts or may present adenomatous characteristics. These instances are probably cases of the exophthalmic syndrome superimposed upon a simple or nontoxic growth. Rarely an exophthalmic goiter may develop secondary changes such as fibrosis, or in the aged, carcinoma, each of which will present the respective macroscopic and microscopic picture.

The Thymus

This organ is enlarged in a considerable percentage of cases, as pointed out elsewhere in this work. Marine and Lenhart state that the degree of hyperplasia varies with the age of the patient, the duration and severity of the symptoms, the state of the patient's nutrition, and other unknown factors. Kocher states that in nearly 50 per cent of cases of Basedow's disease, there is a tendency to tardy hyperplasia or tardy evolution of the thymus.

Parathyroids

Hector Mackenzie asserts that some of the more serious symptoms of Graves' disease are due to atrophy of the parathyroid glands. Rautman claims that the parathyroids are in a state of hypertrophy or hyperplasia. Other observers also present conflicting views.

Pituitary

Though we occasionally find cases of Graves' disease associated with evidences of acromegaly and instances in which the pituitary is affected with a growth or is hyperplastic, the vast majority of reports indicate that this organ as a rule does not present material pathologic changes in the affection.

Suprarenals

Observations on the pathology of the suprarenals are not numerous. Rautman has found a degree of atrophy in his cases. Pettavel, Wiesel and Hedinger (quoted by Roussy), in cases associated with the status lymphaticus, have observed a diminution in the medullary substance of the suprarenal glands in Graves' disease.

Further study may in course of time reveal certain microscopic changes in the suprarenals during the course of exophthalmic goiter, in view of the fact that there are evidences of abnormal function of these organs in a certain percentage of cases.

Nervous System

L. B. Wilson, in 31 cases examined, found hemorrhages and areas of softening in the brain and medulla, and occasionally atrophy and sclerosis of the restiform bodies. The cervical sympathetic presented hyperpigmentation, chromatolysis, and fibrosis. MacCallum does not find changes sufficiently marked to be considered important.

Trousseau discovered a sclerosis of the inferior cervical ganglion with atrophy of the nervous elements. Geigel found both cervical sympathetics in the process of atrophy in a sheath of cellulo-adipose tissue. MacDonnel and Moore have cited a case of fatty infiltration of the inferior cervical ganglion (Roussy).

Though occasionally slight pathologic changes are observed in the nervous system, these are not characteristic, and in the great majority of cases the brain, spinal cord, and sympathetic system present no definite alterations. The lesions are variable, insignificant and inconstant.

Heart

Cardiac hypertrophy, dilatation or both are quite common in Graves' disease, the degree depending upon the severity and duration of the disease and the previous condition of the organ. There are no lesions characteristic of the disease. Microscopically we find evidences of myocardial degeneration resulting from the chronic overaction.

Orbits

Since it is observed that the exophthalmos usually disappears after death, the theories offered to explain this sign are of but relative value. R. Mackinnon, who performed an autopsy on an individual who died of pneumonia, in whom there was an exophthalmos of long standing originally due to exophthalmic goiter, found the retroorbital spaces filled with fat. That the exophthalmos presents on autopsy nothing to explain it but an increased amount of retroorbital fat and in a certain percentage of cases an undue dilatation of the blood vessels, is the opinion of most pathologists.

Pancreas

It has been mentioned that the pancreas is depressed in function by thyroid hyperactivity, and that glycosuria is a common occurrence. In view of this fact, examination by many observers yields evidences of degeneration of the Islands of Langerhans quite similar to the picture presented in diabetes mellitus.

The liver, stomach, intestines, respiratory, cutaneous and genitourinary systems present atypical evidences of thyroid stimulation which, though interesting, are pathologically unimportant.

Spleen and Lymphatics

A study of the spleen has not been seriously attempted in the pathology of Graves' disease. Some observers have reported a moderate splenic hyperplasia.

The lymphatic glands are often found enlarged. This occurs with almost the same constancy as enlarged thymus. The lymphatic tissues, especially of the thyroid, parathyroids, liver, kidneys, bone marrow and intestines, are most apt to be involved. Enlarged tonsils and adenoids often coexist, either coincidental with or as an etiologic factor of Graves' disease.

It seems reasonable to assume that the hyperplasia of the lymphatic tissues of the body, including the spleen and thymus, is at least partly due to the attempt on the part of nature to protect the body against the thyroid toxins and other poisons causing or resulting from the thyroid affection.

CHAPTER IV

PATHOGENESIS OF EXOPHTHALMIC GOITER

The term exophthalmic goiter is an unfortunate one, since it presupposes the existence of a goiter which not always obtains, especially in early cases; it also indicates the existence of exophthalmos, which sign is very frequently absent or late in coming. The term "hyperthyroidism" is not open to as great an objection as that of exophthalmic goiter; but here again we assume that we are completely cognizant of the etiology of the disease. Would that we were! Though many clinicians feel quite confident that hyperthyroidism is the cause of the syndrome, *i.e.*, that the essential symptoms are engendered by an overaction of the thyroid gland, the more modern view does not accept this without reservation, believing the syndrome the result of a disturbance of all the ductless glands of the body and of many other organs, the thyroid being but *an incidental factor.* So that, the term hyperthyroidism is not a fit name for this disease. As for the terms "Graves' disease," "Basedow's disease," and "Parry's disease," these, though not explanatory in themselves, would be fairly acceptable were it not for the fact that it is still a matter of contest to whom belongs the credit for the first description of this disease.

Each of these names has its champions. In 1825, Caleb Parry of Bath called attention to a series of symptoms corresponding to this disease and to him, according to Osler, belongs the credit of its description. In 1835, Graves of Dublin did likewise. In 1840, Von Basedow of Germany published a paper on the subject, and in that country, this disease is known as the "*Basedowische Krankheit.*" Other observers, namely Stokes and Trousseau, Marie, Charcot, and Moebius, also have called attention to various phases of this condition. "Toxic goiter" is a term often employed in certain quarters, as is "thyrotoxicosis," the first indicating the existence of goiter, and therefore open to the aforementioned objection; the second, a more acceptable term, is rather vague in its implications. The most recently applied term to this disease, "dysthyroidism," is probably the most rational, since it does not commit itself to as many errors as the foregoing nomenclature. As it is a generally accepted conclusion that the manifestations of the disease are largely due to an aberration in the quantity and quality of the thyroid substance in the blood, and since it is often observed that evidences of hyperthyroidism are occasionally associated with evidences of hypothyroidism either concomitantly, in alternation, or the latter permanently succeeding the former, the term "dysthyroidism" seems to cover the situation. Dysthyroidism, then, indicates essentially a departure from the normal of the quantity and quality of thyroid secretion within the bodily structures.

However, since in medical, as in other literature, "good usage" facilitates the purpose of an author where strict adherence to severe scientific terms might hinder lucidity of description, we shall in this work confine ourselves to the most common terms employed with reference to this disease, and instead of "toxic goiter," "thyrotoxicosis," or "dysthyroidism," such terms as "Graves' disease," "Basedow's disease," "hyperthyroidism," and "exophthalmic goiter" will be used interchangeably for the sake of convenience.

During the past sixty years, the theories advanced to explain the function of the thyroid gland and the explanations offered to elucidate the phenomena of thyroid disease are as a haystack of speculation in which the needle of truth is still at large. We have delved for generations in the mysteries of the thyroid gland with but few lucid facts in reward for our labors; volumes have been written on the physiology of the thyroid, the pathology, the physiologic chemistry; and above all have many industrious experimenters devoted years of toil in expatiation of their individual theories on the pathogenesis of Graves' disease; but who can tell exactly how near we are to clearing up the mysteries of thyroid physiology and thyroid pathology? Is hyperthyroidism a disease originating in the thyroid gland itself or in some disturbance of the thymus? Do the palpitation and the tachycardia, the trembling of all the muscles of the body, the protruding eyeballs, the cold, clammy skin, the extreme restlessness, the nervous diarrhea, all these constituting the picture of fright, indicate that the cause lies in a disturbance of the emotional balance with secondary thyrotoxicosis, or is the guilt to be fixed on the organs of reproduction? Does the cause lie in a shock to the central nervous system or is it in a derangement of the sympathetic nervous system, especially the cervical sympathetic? Are the suprarenal glands and pituitary body innocent bystanders in the development of the Basedow syndrome or is the entire picture instigated through some specific autointoxication from the digestive organs? What part, if any, does heredity play in the development of the disease? These and dozens of other questions may be asked, but the answers are not forthcoming in spite of the vast amount of literature to be secured on this subject. That exophthalmic goiter and other diseases, eminently diabetes mellitus, arthritis deformans, and occasionally epilepsy, are in a large proportion of cases traced back to a sudden shock to the emotions, especially fright, has led many to believe that the loss of emotional balance is in a large measure responsible for the onset of exophthalmic goiter. To add to the perplexity of this question, we find occasional instances of spontaneous cure of advanced cases of exophthalmic goiter where the syndrome disappeared as mysteriously as it came, and the patient, after having gone the rounds of hospitals and physicians and having given up all hope of recovery, suddenly finds herself improved and becomes healthy and strong. Still more mysterious is the rare instance of recovery through a shock superimposed upon an already existing toxic goiter, exemplified by the following case:

I know of a woman whose enlarged neck and other Basedowian symptoms so preyed on her mind that she was subject to occasional attacks of suicidal mania. In one of these attacks she seized a large knife and tried to "put an end to it all" by cutting her throat. But her large goiter acted successfully as an insulator, and the great vessels of the neck were unimpaired. She slashed herself again and again, only succeeding in severing several veins coursing through the peripheral portion of the goiter, which caused her to fall to the floor in a faint from pain and loss of blood. When discovered, she was taken to a hospital where the wounds healed kindly by first intention. At the same time it was noticed that the swelling which had existed for several years was becoming smaller. Soon the mass was seen to shrink with great rapidity and in three months it was gone, with amelioration of all other symptoms of the disease.

Whatever the remote or predisposing causes may be, one thing seems certain: Graves' disease is directly caused by an oversupply of thyroid secretion thrown into the circulation, and possibly also an alteration in quality of this secretion. In support of this statement, nearly all clinicians agree that any measure directed toward *reducing the formation of thyroid secretion* yields relief.

Though the syndrome of exophthalmic goiter corresponds to the signs and symptoms of thyroid intoxication and may be artificially produced by overdosage with thyroid substance, it is likely that these manifestations are not caused by the thyroid alone, but that other, if not all, remaining ductless glands conspire to produce the same effect. The functions of the ductless glands are interrelated; when one becomes abnormal in structure and function, the others also become abnormal, and it is also evident that because of this ductless gland abnormality, the other systems of the body (the gastrointestinal, nervous, genitourinary, etc.), are variously involved. Stengel very ably sums up the question: "The more one studies hyperthyroidism, the more one realizes that it is the algebraic sum of many morbid processes, some of these arising in the thyroid gland, others in the parathyroid, others in the pancreas or adrenals, or in the general metabolism of the liver itself; and there are evidences that the pituitary body and the ovarian secretion are not unimportant in the interrelationship among those many glands, and not without their influence in the varying expressions of the general metabolism of the body. Hyperthyroidism is not an entity; it is not the expression of a single influence. It is the manifestation of a lack of equilibrium in the relationship of many glands of the body, and this equilibrium may be influenced by an increased or diminished function of any of these related ductless glands. We must, therefore, realize that when we consider a typical form of Graves' disease, the thyroid may be the least at fault, and furthermore, we must realize clinically that where tachycardia is present, we should think of some disturbance of internal secretion, and not attribute it to mere nervousness, thus dodging the responsibility of a more accurate diagnosis. When nervous irritability and change of disposition occur, where formerly reasonable patients present a veritable chorea of intellectual functions, we should not attribute it to neurasthenia, but realize that they are suffering from internal poisoning which we have been accustomed to consider as part of the symptoms of Graves' disease, and which we would readily recognize if the full picture were present with exophthalmos, goiter, and tachycardia combined. So long as the goiter or exophthalmos is present, or the tremor with the tachycardia, there is no question that the patient will soon be placed with the proper clinical group, but it is in these cases in which the symptoms which we formerly considered cardinal are absent, or where they are present only in slight degree, that we usually fail to recognize the chief disturbances as one of upset equilibrium among the ductless glands."

The subject of pathogenesis of exophthalmic goiter is so vast were it treated in detail, that we are compelled to abbreviate considerably to avoid an expenditure of valuable time in the perusal of chapters of mere speculation. A cursory survey of the most important views will here suffice for practical purposes. Let us divide the subject matter into (A) predisposing factors; (B) exciting factors. This classification is one of convenience only as there is probably a combination of causes operative in any given case.

(A) Predisposing Factors

Geographical Distribution.—Though simple goiter occurs quite commonly as an endemic disease in certain parts of the world, as for example, in Switzerland, France, and Italy, and is comparatively rare in the plains of North Germany, the Netherlands, and in North America, this can not be said of exophthalmic goiter. Hyperthyroidism is little, if at all, influenced by geographical location, and probably not etiologically related to simple or atoxic goiter. Indeed, Graves' disease is rare in districts where ordinary goiter is common. Among 1,000 cases of goiter seen by Dr. Savage (quoted by Berry) in a goitrous district in the north of England, there was not a single case of Graves' disease. The experiences of Montoya Y. Florez and James Berry confirm this statement. It is my opinion that this is probably due to the more obtuse emotional mechanism existing in the inhabitants of goitrous districts. Though it is said that Graves' disease is more common at the sea coast than elsewhere, we have no statistics to prove this assertion.

Heredity.—The presence of a neuropathic tendency (asthma, hysteria, epilepsy, migraine, insanity, etc.) has often been demonstrated in these cases. Observing internists are often impressed by the frequency with which these conditions occur interchangeably. A parent of unstable emotional balance or one excessively high-strung is apt to have a child susceptible to chorea or epilepsy, whose child in turn may develop hyperthyroidism in the course of its existence. It is not uncommon to find an apparent direct inheritance of the disease itself. Rosenberg reports a family in which a grandfather, father, two aunts, and two sisters were afflicted with hyperthyroidism. Oesterreicher reports eight of a family of ten suffering with the disease. Bumstead reports a family in which four sisters suffered with Graves' disease of varying degree. In one of my cases there is a history of the mother and grandmother having suffered with hyperthyroidism. In 34 private cases of Hector Mackenzie, the disease evinced a tendency to show itself in the same family. A. Ricaldoni states that in one family a young man, his mother and his aunt all had exophthalmic goiter. In another, one brother had exophthalmic goiter and the other myxedema. In a third family it was possible to trace a pigmented retinitis and a dysthyroidism through three generations. The conditions were transmitted independently. The author believes that there is a constitutional dysthyroidism which may evolve in opposite types of thyroid malfunction.

Age.—Though usually occurring after puberty or during the period of greatest sexual activity or active adult life, Graves' disease has been seen in the extremes of ages. The disease is rare in the very young; my youngest case was a girl of thirteen. It is relatively more common in the aged; I have this year attended a woman of sixty-two whose hyperthyroidism, superimposed upon a simple goiter of many years' duration, had begun three years ago and whose thyroid was now undergoing malignant changes. I have at this writing under my care a man of sixty with Graves' disease of moderate severity, of approximately nine months' duration.

Sex.—Graves' disease is most common in women, but when this occurs in a man the progress is more rapid and the prognosis graver. Eshner, in a series of 200 cases, shows 161 females. This frequency in females as compared to males may be explained by the greater complexity and more profound changes occurring in the female sexual organs during the course of her existence. It is widely recognized that the thyroid gland is intimately related to the organs of procreation, and that changes incident to puberty, menstruation, childbearing, and menopause are of necessity accompanied by changes in quantity and quality of thyroid secretion. A sluggish thyroid function in girls is coincident with a retardation in the development of the ovaries, with postponed menstruation and occasionally menorrhagia. The uterus and adnexa are in these cases underdeveloped. The administration of thyroid extract serves to check the menorrhagia.

Race.—Graves' disease is most common in the Caucasian and Mongolian races. Though simple goiter is most common among negroes, hyperthyroidism is rarely if ever seen in this race. Of the many inquiries made of noted men throughout the country, only one clinician has seen a case of Graves' disease in a negro. My observation indicates that the Hebrew has a rather high susceptibility to hyperthyroidism. The reason is probably the same as that attributed to the increased prevalence among Hebrews of diabetes mellitus and neurasthenia—namely, a high-strung temperament.

Iodine Basedow.—Iodine applied to the neck and the prolonged administration of the iodides internally, will at times give rise to thyroid hyperactivity in persons whose thyroid function had been entirely normal, and occasionally Graves' disease will develop through this cause. Hollervorden states that in his experience the administration of iodides was beyond question the onset of the acute phase of exophthalmic goiter in no less than 25 cases out of the one hundred which he discusses.

Whether to use iodine in exophthalmic goiter is, however, still an undecided question. Occasionally, instead of aggravating a case of exophthalmic goiter, the iodides seem to cure the patient. This does not occur often, but it *does* occur. The beneficial effects of the iodides in occasional instances of exophthalmic goiter have been observed by some of the world's ablest clinicians, despite the fact that iodine therapy is harmful in the vast majority of cases.

The Infections.—Measles, whooping cough, mumps, scarlet fever, diphtheria, malaria, rheumatism, influenza, phthisis,—in fact, any infectious intoxication may lead to hyperthyroidism. E. H. Reede mentions several instances in his experience in which mouth infection has been accompanied by thyroid abnormalities, particularly exophthalmic goiter, and in which marked improvement followed treatment of the infections. Syphilis is a condition which must always be borne in mind, and a Wassermann test must be made in all cases where there is the slightest suspicion of its existence. Tuberculosis is caused by, and associated with Graves' disease, to say nothing of the frequency with which the two conditions are confused. This latter is not surprising in view of the fact that both diseases are capable of presenting an afternoon rise in temperature, profuse sweating, flattening of the chest and marked wasting of the body. The wasting and diminished respiratory expansion occurring in Graves' disease frequently lead to an active phthisis, especially where there has been a latent focus. Adolphus S. Knopf often meets with cases of young girls suffering with both enlarged thyroid and pulmonary tuberculosis. Bialokur finds that in 10 per cent of his tuberculosis cases there are symptoms of exophthalmic goiter,—predominately seen in women (one man to ten women). Symptoms of excessive thyroid functioning may occur in the very incipient stage of pulmonary tuberculosis and seem independent of the gravity of the case and of the age. Bialokur is of the opinion that symptoms of Basedow's disease may indicate the existence of a latent tuberculous infection and that successful treatment of the exophthalmic goiter symptoms may improve the pulmonary process. Swelling of the thyroid occurs in 50 per cent of early cases of secondary syphilis (Engel-Reimers). Late secondary and tertiary manifestations of syphilis in the thyroid are said to be rare. These cases of goiter respond very readily to local and internal iodine therapy.

Diseased tonsils, adenoids, and nasal sinuses, and infections of the gums and teeth are now recognized as strong predisposing factors. Now and then a case of hyperthyroidism will be cured by the removal of such tonsils and adenoids, nasal polyps, or the proper treatment of a chronic sinusitis. B. R. Shurley calls attention to the physiologic and pathologic relation of the tonsils to the thyroid gland and states that he has obtained beneficial results in a series of tonsillectomies for the relief of recurrent tonsillitis and quinsy attended by incipient typical and atypical exophthalmic goiter. In his experience, the laryngeal muscles often show some insufficiency, varying with the size of the goiter; hyperemia of the pharyngeal, bronchial and pulmonary mucosa is common in exophthalmic goiter; if the gland is hard, it may cause tracheal cough. He believes that more rhinologists and otologists should bear in mind the close relation between the thyroid gland and the organs in their special field.

R. C. Hammill presents the case of a woman forty-one years old with a negative family history, who has had tonsillitis since the age of six. Enlargement of the thyroid was noticed at the age of eighteen, when it was much larger than at the present time. She had at that time puffiness of the eyes, shortness of breath, and was very nervous. Then the symptoms ceased until at twenty-four she had another attack and was afraid to walk because of precordial distress. Since then excitement caused severe emotional strain. At the present time, she has the symptoms of exophthalmos, Stellwag's positive, Moebius' negative, tremor of outstretched hand, perspiring freely under axilla, flushed skin around neck and over upper chest, marked dermographia, swelling of the isthmus and right lobe of the thyroid. Marked palpitation of the carotid. Blood pressure

150-78. Temperature normal, blood count normal. Pulse 115-125. Tonsils enlarged; from the right pus was ejected. Hammill thinks that the tonsils either became infected with a microorganism whose virulence varied from time to time or else they became a *locus minoris resistentiæ* to microorganisms such as we are constantly taking into our mouths, and hence reinfected at frequent intervals. He thinks that tonsillar infection stimulates the thyroid in many cases, as it produces acute inflammatory rheumatism and chorea in others.

In a personal interview, Sajous told me that in his experience also, very often the tonsils are discovered to be the etiologic factors in goiter formation, both simple and toxic, and that the removal of the offending tonsils often leads to cure. Several cases of mine seem to confirm this view.

Miscellaneous.—Thyroiditis, either primary or secondary to some infectious diseases, often leads to a hyperactivity of the thyroid, a surcharging of the blood with a surplus of its secretion and a typical Basedowian syndrome.

Traumatism to the thyroid has likewise been known to bring about a gradual onset of the disease.

For the sake of completion, we must here mention simple or nontoxic goiter as a cause of a typical or atypical hyperthyroidism (Basedowian goiter).

Here it must be recalled that mere pressure of a thyroid mass upon the cervical sympathetic may be followed by a few of the signs and symptoms of Basedow's disease, which, though significant of the affection, must be classified under the appellation of "false Basedow," often with difficulty differentiated from true Graves' disease.

Having enumerated a few of the possible indirect or predisposing factors thought to be responsible for the production of the Basedowian syndrome, let us examine some of the important direct or exciting factors. Most of these consist of theories advanced by men of science who have given the subject considerable thought.

(B) Exciting Factors

The following summary of ideas concerning the etiology of exophthalmic goiter is of interest:

Graves: Exophthalmic goiter is a dyscrasia of scrofulous and circulatory origin.

Basedow: The disease is a general dyscrasic malady.

Marsh, Pral, Maumann, Heusinger: It is a malady of the heart.

Friedreich believes that the disease is caused by an enlargement in the caliber of the coronary arteries of the heart, and this, resulting in tachycardia, would lead to nervous phenomena.

Stokes considers the affection as one of cardiac neurosis.

Keben, Aran, Trousseau, Charcot believe it to be a neurosis of sympathetic localization.

Eulenberg, Panas, and others: A neurosis of central origin.

Gauthier, Moebius, and their followers: A disease of thyroid origin.

That Graves' disease is of bulbar origin was suggested by Tedeschi and Warburton who, by making section of the restiform bodies produced a syndrome of symptoms including an increased vascularity of the thyroid, tachycardia and exophthalmos. The syndrome did not occur, however, if the section was preceded or accompanied by thyroidectomy.

According to Crile, the thyroid hyperplasia is not a cause but a concomitant effect of exophthalmic goiter. In support of this view, he points out that only a small percentage of cases of thyroid hyperplasia is associated with Graves' disease, for hypertrophy of the thyroid is chiefly incident to pregnancy, to adolescence, to many infections, especially tuberculosis, and to cretinism. He claims that hyperplasia of the thyroid is no more the cause of exophthalmic goiter than it is the cause of pregnancy, of tuberculosis, or of adolescence. In each and all of these conditions hyperplasia is an effect, not a cause. Crile believes exophthalmic goiter is the result of a disease of the "kinetic system."

The kinetic drive, according to Crile, is the excessive excitation of the kinetic system. The kinetic system is the brain and the muscles, together with the suprarenals, liver, and thyroid.

"The organs," says Crile, "which from moment to moment vary and control, accelerate and retard the driving force of the *brain,* are the *suprarenals,* the pacemaker of the kinetic system is the *thyroid,* and the final act of adaptive energy transformation is performed by the *muscles.*"

The activators of the kinetic system are: physical injury, heat and cold, emotions, infection, autointoxication, pregnancy, excessive food, poisons and other factors.

Crile tells us, "perhaps the most typical of the kinetic diseases is exophthalmic goiter. In exophthalmic goiter the kinetic system is driven by a continuous activation, because in this disease there has been established a pathologic interaction between the brain and the thyroid, whereby the threshold of all stimuli is kept continuously low * * * The principal phenomena of exophthalmic goiter are identical with the leading phenomena of any other kinetic drive of a corresponding degree of intensity, and may be duplicated by fear, anger, sexual excitation, physical exertion, overwork or acute infection. Conversely, many of these activations cause hyperplasia of the thyroid. Thus fear, anger or sexual emotion may cause temporary enlargement of the thyroid; there is hyperplasia of the thyroid in pregnancy, in chronic infections, and perhaps in intestinal autointoxication as well."

Marimon presents arguments to sustain the view that myxedema and exophthalmic goiter are due to the same cause—insufficient thyroid functioning. The former is the result of defective utilization of the iodine assimilated from the food and metabolized in the liver or elsewhere. Exophthalmic goiter, on the other hand, is the result of injury from iodine getting into the blood insufficiently metabolized.

This assumption explains the coincidence of myxedema and exophthalmic goiter, which he has frequently observed and which it is impossible to explain by the current theory that myxedema is the result of hypothyroidism and Basedow's disease of hyperfunctioning. As he remarks, a glass can not be full and empty at the same time.

While Schiff was the first to attempt to combat thyroid deficiency by transplantation experiments in dogs in 1859, it remained for Reverdin and Kocher, in 1882, to publish their observations on patients from whom the thyroid had been removed and thus call the attention of the medical world to the importance of the gland. Within a few years it was recognized that the underlying cause of cachexia strumipriva, sporadic and endemic cretinism and myxedema, was the same in all, viz., the deficiency or absence of the thyroid; on the other hand, hyperfunction of the thyroid gland produced Graves' disease, though conclusive demonstration of an excess of thyroid secretion in the blood of those patients has not been furnished. Further experimentation led to more decisive conclusions (Roussy).

Pfeiffer (1907), having grafted into the spleen of a dog a fragment of Basedowian thyroid, saw produced a severe tachycardia with cardiac failure terminated by the death of the animal.

Schoenhorn (1909), provided with such material as seven exophthalmic goiters and sixteen ordinary goiters, has been able in the laboratory of Professor Gottlieb to examine comparatively the cardiovascular action of the extracts of the two kinds of goiters. He has not found any essential difference between the Basedow and the ordinary goiters, excepting that the Basedowian extract exerted an action a little stronger than that of the ordinary goiter.

Iscovesco (1910) has drawn from the thyroid of the sheep lipoids of two types. In animals, the one caused tachycardia, convulsions, emaciation; the other, exophthalmos.

Gley (1911) and Cleret have stated that experimentation with serum of the Basedowians was not similar in results to experimentation with thyroid extract. They determined some acceleration of the heart, weakening of the systole, a diminution of the excitability of the moderator nerves of the heart, and after an immediate elevation, a lowering of the blood pressure.

Baruch (1912), on injecting into the peritoneum of animals extracts of simple goiters, has provoked tachycardia, emaciation, rise in pulse, diarrhea, sometimes also exophthalmos.

But the most remarkable experimental results are those which were obtained recently (1911-1912), by Klose, Lampe, and Liesegang. The conditions in which these authors have placed themselves and the rigorous method with which their experiences appeared to have been conducted perhaps explain their success. At first they thought that in order to produce experimentally the Basedowian syndrome, it was necessary to choose animals susceptible to a development of this syndrome spontaneously. Now, only the dogs and the horses of pure race are in this class. They operated, then, on fox-terriers of pure race. Then they employed the extract of fresh Basedowian thyroid and injected it into the external jugular vein (1 c.c. to the kilo. of animal). This resulted in a sharp rise in temperature, an extreme tachycardia with irregular pulse, agitation, general tremor, a jerky respiration, considerable exophthalmos, intestinal symptoms, albuminuria, glycosuria, and a lowering of the blood pressure. The symptoms were effaced in five days and the animal grew very thin. New injections reproduced the same picture, without anaphylactic phenomena. Stronger doses provoked a graver symptomatology, light doses an incomplete syndrome.

Let us now examine a few of the *most popular* and attractive theories advanced to explain the syndrome of Graves' disease. They are:

The Theory of Intestinal Toxemia.—The view that exophthalmic goiter is due to infection from the gastrointestinal tract is held by many observers, notably McCarrison, Gaylord, Epstein and Thompson, and is seemingly confirmed by the experimental evidence of Halsted and Hertoghe, and the clinical evidence of Sir Arbuthnot Lane. In support of this view, it is suggested by Blum that albuminoid toxins are rendered innocuous by the iodization of thyroid activity, and that an undue quantity of these poisons existing in the intestines would demand a compensatory increase in thyroid activity, hence, hyperthyroidism.

The effect of a gastrointestinal toxemia on thyroid activity is apparently emphasized by a case of Sir Arbuthnot Lane (quoted by McCarrison). The patient was a girl, nineteen and a half years of age, suffering with advanced Graves' disease of eighteen months' duration. The previous medical history included attacks of rheumatism, chorea, tonsillitis, and an attack of nervousness of six months' duration. The symptoms on admission to Guy's Hospital were emaciation, abdominal pain, attacks of nausea and vomiting, exophthalmos, tachycardia, severe palpitation, extreme tumultuousness of the heart's action, pulsation of the great vessels, great weakness, marked tremor, nervousness, dizziness, headaches, subjective sensations of heat, suppressed menses, and many minor symptoms. Albuminuria and glycosuria were present. X-ray examination revealed the presence of a greatly dilated stomach with pyloric spasm, an elongated duodenum, and a state of chronic irritation of the colon resulting in an unduly rapid emptying of its contents. Lane performed a gastrojejunostomy and removed an anchored appendix which exerted a most marked control upon the ileal effluent, and freed a very light terminal kink at the junction of the ileac and pelvic colon. A few months later the patient became entirely well and normal, with the exception of a small goiter which was probably due to fibrotic changes.

Such observations seem to prove that at least *some* cases are caused by gastrointestinal disturbances, especially fecal retention. X-ray examination and an examination of feces must not be omitted in seeking for the etiology of exophthalmic goiter.

The Neurogenic Theory.—Oswald emphasizes the fact that all persons do not respond to a hypersecreting thyroid with symptoms of Basedow's disease; a predisposition to this disease is necessary, and the genetic factor lies in the nervous system. It is in this manner that the thyroid secretion causes Basedow's disease in persons with an impaired nervous system. Mental strain or continuous excitement is an exciting cause. The primary cause is a weakened nervous system, and the struma is a secondary symptom resulting from the thyroid secretion. The thyroid receives its impulse from the nervous system of which it is physiologically a part and acts through a specific substance as an intensifier.

Persons of a sensitive, nervous, or high-strung temperament are highly susceptible to the disease, that is, they are prone to excessive thyroid activity. Emotional disturbances, such as worry, anxiety, excitement, and prolonged physical or mental strain are predisposing causes. There is a remarkably clear indication that traumatic shock or fright is capable of bringing on Graves' disease in persons previously possessing perfect health. In one of my cases, the man was seated in his back yard reading a newspaper, one fine, warm day, when a "friend" suddenly approached from the rear and poured a cup of ice water down his back. The sudden fright resulted in a well-marked picture of hyperthyroidism, two months later. In another case, the syndrome asserted itself some weeks after extreme worry following the death of the patient's mother; in another (a woman of fifty) the symptoms gradually appeared after a train accident.

Sajous reports a case due to an accident and rapidly proceeding to recovery under medical treatment, which promptly recurred after a second accident, although the patient did not suffer traumatism.

Beebe had as patients four men who developed severe hyperthyroidism during their experiences in the army serving in the Philippine Islands. They were in excellent health on entering the army and could definitely date their trouble to a particular campaign. Later, at the time of the Kishineff massacre in Russia, Beebe states that patients who had been subjected to the horrors of this experience came to New York City with severe hyperthyroidism, the incidence of which they definitely dated from the fright and hardship then endured. He states that the San Francisco earthquake produced similar cases, and saw three patients with this condition developed from the Triangle Shirt Waist Co. fire. "A proportion of cases may be precipitated by some accidental circumstance, such as a train disaster, a fall from a horse, or such circumstances as seduction, attempted rape, or the excitement and strain of war * * * fright, mental distress and worry, business or social cares, unfortunate love affairs, violent emotion, and mental and physical exhaustion with loss of sleep such as occurs amongst soldiers in the trenches" (McCarrison).

And so, again and again do we obtain similar histories pointing suggestively toward the emotional theory. Says Mackenzie: "Fright, intense grief, and other profound emotional disturbances have been recognized as causes of this pathologic condition, but I do not think that sufficient attention has been paid to the very close connection between the chronic symptoms of Graves' disease and the more immediate effects of terror. The description given by Darwin and Sir Charles Bell of the condition of man in intense fear might almost have been written with regard to a sufferer from this disease. The heart beats quickly and violently so that it palpitates or knocks against the ribs. There is a trembling of all the muscles of the body. The eyes start forward, and the uncovered and protruding eyeballs are fixed on the object of terror. The surface breaks out into a cold, clammy sweat. The intestines are affected. The skin of the face is flushed, down over the neck to the clavicles

* * * Of all the emotions, fear is the most apt to induce trembling. There are one or two of the minor symptoms of Graves' disease whose independent occurrence is well known. These are the pigmentary changes in the skin and hair, the falling out of the hair and epistaxis.

"Such being the condition resulting from severe terror, we have only to imagine the condition to become prolonged by a failure of the nervous system to recover its balance and right itself, and we have a more or less complete clinical picture of Graves' disease. We have all the well-known symptoms,—trembling, palpitation, flushing, sweating, exophthalmos, relaxation of the bowels. There is no information that I know of in regard to the enlargement of the thyroid gland under the influence of profound emotional disturbance. All one can say on that point is that the enlargement which takes place in these cases where the symptoms develop rapidly after such disturbance makes it probable that this is actually the case. If this be so we have had associated with one another, probably as long as the human race and its ancestors have existed, the symptoms which we find in Graves' disease. The existence of a certain abnormal condition of the nervous system having been once established, we know how in time, it becomes dissociated from its existing cause, rises to independence as a disease in its own right, and may require only a minimal incitement to set it off. In many cases the disease is started again by severe mental shock; probably in a good many cases it is the expression of an unconscious memory of the individual of some such shock in an ancestor.

"Such is what I would suggest to you as the origin and development of this very curious disease. It is likely that the alteration of the function of the thyroid body, whose importance in connection with the nutrition and the transmission of nerve force has been amply demonstrated, has a good deal to do with many of the secondary symptoms to which I have called attention, but the real disease is a widely distributed derangement of the emotional nervous system."

In this connection it may be remarked that soldiers under the unaccustomed physical and emotional strain are particularly susceptible to thyroid hyperactivity. The recent European war has engendered thousands of such instances, many of which have been erroneously termed "shell shock." These men are exceedingly nervous, lose weight rapidly, and many complain of distressing palpitation and insomnia. Hysteria, melancholia, hallucinations and the manias are common. On examination, the thyroids of most of these men are palpably increased in size, and though the number of cases of exophthalmos is small, tachycardia, arrhythmia and vasomotor instability are very common.

Injury to the thyroid gland seems to be the exciting cause in rare instances; shock of operation elsewhere upon the body has also been followed by typical evidences of hyperthyroidism.

Shock, worry, anxiety, prolonged mental strain and the like, cause in one patient diabetes mellitus, in another arthritis deformans, in a third insanity, here epilepsy, there hyperthyroidism. Under such etiologic influences how can we foretell which patient is apt to become a sufferer from one or the other of these diseases? We may only suggest that a given cause affects a person in the most vulnerable part of the economy, producing a corresponding alteration in function,—a diminished, an increased, or perhaps an irregular glandular or hormone activity. And in the case of hyperthyroidism, there is probably a generalized disturbance in the harmony of interrelationship between the ductless glands, which conspires to produce a hyperactivity of the thyroid body.

It is of interest to note the views of my esteemed senior, Dr. Charles E. deM. Sajous, the pioneer in endocrine research, whose remarks are authoritative. In an address before the American Therapeutic Society, June 6th, 1919, he said in part: "There have long been * * * two main theories regarding exophthalmic goiter, 1st, that it is due to excessive thyroid activity; 2nd, that it is a nervous disorder.

Time has shown, however, that, as is often the case with strong and well-sustained hypotheses, both were correct and more or less interwoven. Moreover, other ductless glands have been found to participate in the morbid process, the adrenals and thymus in particular. These fundamental facts being no longer disputed, we are brought to inquire into the cause of these morbid phenomena. Why is the thyroid gland overactive and in some cases enlarged? Why is the nervous system so deeply involved in the process? Why are all the body structures the seat of destructive erethism?

"We now know that various toxins originating from the intestines, pyogenic disorders of the tonsils, nasal and the faucial cavities, peridental and gingival pyorrhea, gastroptosis with prolonged retention of ingesta, etc.—may underlie the morbid process. We know also that when these disorders are carefully sought and as thoroughly eradicated, all the symptoms due to hyperthyroidism improve and often disappear. These various sources of general intoxication obviously constitute the fundamental factor of the disease and yet, most writers, particularly those who speak of 'symptomatic' treatment, fail to refer to them. The reason is not far to seek: Some overlook the toxemia. Others, though admitting it, fail to take into account the one factor which elucidates the whole morbid process, viz., that it is in defending the body against intoxication that the thyroid body becomes abnormally active.

"What are, briefly, the facts that point to the defensive function of the thyroid?

"Summarizing, the observations of many physiologists, pathologists and clinicians have clearly shown: 1, that removal of the thyroid apparatus reduces markedly the antitoxic and bactericidal properties of the blood, and that these properties are restored by giving thyroid gland; 2, that the blood and urine are rendered more toxic by removal of the thyroid apparatus, but that this unusual toxicity is removed by giving thyroid gland; 3, that animals are rendered more susceptible to infection by removal of their thyroid apparatus, but that they can be protected against certain toxins, particularly those capable of causing a febrile reaction, by giving thyroid gland. My own labors have indicated that this antitoxic action of the thyroid secretion was similar to that attributed by Sir Almroth E. Wright to opsonins, and also that it was a component of the systemic autotoxins or alexins; this was confirmed by several European experimenters, Fassin, Stepanoff and Marbé. Frugoni, Grixoni and many other clinicians, including myself, have also conclusively found that thyroid medication promptly influenced favorably both autointoxications and infections.

"Beebe * * * recognizes * * * that 'if the thyroid secretion is an important element in the defense against infections, it is not impossible that it is stimulated to overactivity when occasion demands, and if the stimulus be often repeated, it may produce changes which we recognize as pathologic. Through the repeated stimulus to overactivity the gland has become hypertrophied, and its heightened function continues long beyond the stimulus which called it forth.'

"Others have attributed the antitoxic power of the thyroid to the active metabolism it provokes. But this in no way weakens my view as Beebe defines it, 'that the mechanism of the defense against infections depends to a degree on thyroid function.' It only explains in another way the manner in which the defensive reaction is carried out. The truth of the matter, the details of which I can not develop here, is that the defensive function is part and parcel of the metabolic process, since it is by subjecting toxins, bacteria, etc., to catabolism, precisely as it does in breaking down fats and albumins, that the thyroid secretion carries on its protective rôle. Indeed, Plummer recently stated that 'the thyroid hormone is fundamentally a part of the catabolic process of higher animal life.'

"Now, as regards the influence of excessive mental stress, fear, anger, etc., upon this process, Vas, Mann, Lambert, Lugaro and others long ago showed that nerves fatigued by stimulation more or less rapidly lost this substance (adrenalin), quite in keeping with Crile's more recent clinical views, and with those of Cannon. Briefly, fright, anger, etc., bring about disintegration of the nerve cell, by subjecting it to violent stimulation, which means excessive metabolic activity. And it is here that the primary toxemia or cause of exophthalmic goiter in these cases appears, *e.g.*, excessive metabolism of the nerve cell is known to produce phosphoric acid, cholin, and also a substance known to be particularly poisonous, *neurin,* a body closely allied to muscarin, especially. So sensitive is the thyroid gland to the latter poison, in fact, that it was once believed that the one function of the organ was to destroy neurin as fast as formed. In the light of these facts, therefore, we again realize that a poison, though neurogenic this time, can become the primary cause of the disease.

"But why, the excessive stress due to fear, rage, etc., once terminated and entirely appeased, does the morbid process continue? Why do all the morbid symptoms, particularly those of nervous origin, persist? This is due to a vicious circle. The thyroid, powerfully stimulated to react against the intoxication, itself becomes a destroyer of the nerve cell. This becomes intelligible when we recall that besides the chromatin, the nerve cell is likewise rich in fatty substances, lecithin (containing stearic, palmitic or oleic acid) in particular. If we now recall the familiar fact that thyroid gland first attacks fats, breaking them down sooner than any other tissue, we can realize why it is that excessive thyroid activity so actively disturbs the nervous system. Briefly, *a severe mental stress*—fear, rage, deep grief, etc.—*causes excessive catabolism in the nerve cells, and the excretion by them of highly toxic wastes, including neurin; these poisons by provoking a defensive reaction of the thyroid, cause it to break down fats, including the fatty components of the nerve-cells, thus establishing a vicious circle, by perpetuating the catabolism of these cells and the formation of poisons.*

"This accounts for the severity of such cases, unless, as we shall see, they are treated, not symptomatically, but in such a way as to arrest the excessive thyroid activity. It accounts, moreover, for the well-founded contention by many authorities, that exophthalmic goiter is a nervous disease. Our regretted fellow-member, Prof. Putnam, of Harvard, who passed away a few months ago, was convinced that this view was the only one that explained its symptom complex. The conception submitted in these pages indicates that he, as well as the advocates of the thyroid origin, were right, the actual morbid process in reality encompassing both conceptions."

Sympathetic Theory.—The theory that the cervical sympathetic ganglia are responsible for exophthalmic goiter is one of the oldest. Koeben, in 1855, was the first to describe it. Claud Bernard's experiments on the sympathetic and vasomotor nerves were largely responsible for this theory taking a strong foothold in the minds of observers. Then followed the observations of DeGraefe, Charcot, Aran and Trousseau. This latter observer, according to Roussy, declared, after an autopsy revealing a diseased inferior cervical ganglia: "The functional symptoms of Graves' disease originate from the passive congestion of the great sympathetic, or perhaps, from a persisting structural lesion of the ganglia of this system."

That any agency causing continuous excitation of the sympathetic nervous system may give rise to a syndrome closely resembling that of Graves' disease has been proved by competent observers. Canon, in 1916, fused in six cats the anterior root of the right phrenic nerve with the right cervical sympathetic strand. This increased the pulse rate, the basal metabolism (100 per cent), caused diarrhea and made them excitable. In two that died of the disease, the cortex of the adrenals was greatly enlarged.

L. B. Wilson, in 1918, found the goat to be an exceptionally favorable animal for the study of thyroid problems on account of the close resemblance of that gland to that of man. Studies were made in 19 cases. The superior cervical sympathetic ganglia were exposed and stimulated either electrically or by injections of various sorts of bacteria. It appeared that irritation of the ganglia may produce histologic pictures in the ganglia themselves and in the thyroid, which parallel those found in various stages of progressive and retrogressive exophthalmic goiter. This evidence supports the suggestion which Wilson has previously offered that exophthalmic goiter is due to overstimulation of the thyroid gland *via* the nerve supply and as a result, usually, of a local infection in the cervical sympathetic ganglia.

The supposed *modus operandi* of the sympathetic theory is variously explained by different authors. Koeben, over sixty years ago, expressed it very simply, stating that "the syndrome is due to compression of the nerve trunks by the thyroid tumor." The modern view, as presented by Roussy, seems to be the following: Excitation of the cervical sympathetic gives rise to exophthalmos and tachycardia—two of the principal signs of Basedow's disease; simultaneously with these are produced pupillary dilatation, flattening of the crystalline lens, increased intraocular tension, and such vasomotor phenomena as constriction of the vessels of the conjunctiva, iris, tongue, lips, cheeks, etc. In commenting upon these phenomena of cervical sympathetic irritation it must be said that dilatation of the pupils and pallor of the face are *not* evidences of Graves' disease. To produce such other manifestations as dilatation of the vessels of the neck and of the thyroid, the inverse experiment must be made, that of *section,* bringing about paralysis of the cervical sympathetic. But when this is done, instead of exophthalmos, we produce retraction of the eyeballs. Thus, says Roussy, although excitation and paralysis of the cervical sympathetic give rise to contradictory phenomena, nevertheless the syndrome of Basedow's disease lends itself to both of these opposed clinical pictures. All the adherents of the sympathetic theory have striven to solve this problem but have not yet succeeded. Finally, says Roussy, we find it difficult to accept seriously the theory that the cervical sympathetic is responsible for the syndrome of exophthalmic goiter when the thyroid theory has so much in its favor. The most powerful argument against it is that it does not explain all the facts in the clinical picture. We fail to see much justification of the sympathetic operation to favor its performance. According to Jaboulay, it succeeds especially in those who have little or no goiter and are perhaps not at all affected by true Graves' disease.

G. Barker reminds us that symptoms of sympathetic irritation may be produced by amines of putrefactive decomposition of proteins or amino acids through bacterial action, the most common source of which is the gastrointestinal tract.

Thymus Theory.—Hart, Garre, Capelle, and Bayer are inclined to believe that the thymus gland is largely, if not wholly, responsible for the Graves' disease syndrome.

Nordman thinks that whenever the thymus is enlarged, hyperactivity of the thyroid is apt to occur. Of eighteen operations on Graves' disease, three died, a man of forty-eight, and two women of twenty-eight and twenty-five years. In each of these fatal cases there was an enlarged thymus, which fact causes him to conclude that the presence of an enlarged thymus was responsible for the fatality.

Kocher finds that in 50 per cent of his fatal cases there is hyperplasia of the thymus gland. Rautman finds the thymus usually involved in Graves' disease, and often, changes in the other endocrine glands.

Sinorzersky, from a study of 20 cases of exophthalmic goiter with the object of determining the etiologic influence of the thymus, concludes that the latter is beyond a doubt largely responsible for the production of the former. He discovered that direct x-ray treatment of the thymus gland resulted in an amelioration of the Graves' syndrome.

Bircher implanted in five dogs, in the peritoneal cavity, fragments of human hypertrophied thymus, but not Basedowian. He thus obtained a syndrome of Basedow characterized by agitation, tachycardia, exophthalmos, soft goiter, glycosuria and a transitory lymphocytosis. The tachycardia lasted more than three months. The exophthalmos which attained its maximum at the end of 20 days slowly disappeared thereafter. The goiter persisted.

Again, "Basch, Matti, Gudernatch and others claim that they have demonstrated this relationship and believe that the thymus has an inhibitory action on the thyroid, adrenals, gonads, spleen and pancreas.

"Heidinger found 7 cases of enlarged thyroid in 12 cases of thymic death in the newborn. Garre and Capelle found 95 per cent of fatal cases of exophthalmic goiter to have enlarged thymus * * * Mackenzie noted that in thirty-six postmortem examinations of cases of exophthalmic goiter, the most constant feature next to thyroid enlargement was the presence of an enlarged or persistent thymus. Hart believes that there is a pure thymogenic form of exophthalmic goiter." (M. B. Gordon).

The percentage of exophthalmic goiter in which the thymus is said to be enlarged varies with individual experiences. Barry claims thymus enlargement in 100 per cent of cases; Matti, Capelle, and Bayer, 70 per cent. Halsted finds that from the postmortem examination of cases of exophthalmic goiter that have died of intercurrent disease, it was discovered that the thymus gland is persistent in about 82 per cent of them; and in those cases that have died of heart failure after operation, enlargement has been found in about 95 per cent. At the Johns Hopkins Hospital there has been only one opportunity to make a necropsy on a patient with Graves' disease who died after operation. In this instance a long thick thymus gland was found tapering out from near the top of the manubrium sterni to the auricles of the heart. From facts gleaned at the autopsy table, from experiments on animals, and above all, from the results following primary thymectomies, Halsted has convincing evidence that the thymus gland may play an important part in exophthalmic goiter, and in some cases assume the title rôle. Some of the most puzzling features of the disease are made possible of interpretation by the discovery of the influence which the thymus may exert.

On the other hand, seemingly negative deductions are not lacking. In an attempt to determine whether an excess of the product of thymus activity in the circulating blood could cause exophthalmic goiter or not, experiments were made by N. B. Eddy on rabbits. Two rabbits served as a control. Three rabbits were given hypodermic injections of thymus substance in the proportion of 5 mg. per kilogram of body weight, and three in the proportion of 10 mg. per kilogram. Forty injections were given to each rabbit. There was no evidence of the production of symptoms characteristic of exophthalmic goiter by the thymus gland substance employed in either group of rabbits. These experiences are confirmed by those of Gebele whose results were negative even though the transplanted thymus was of Basedowian origin.

In reviewing the various opinions deduced from experimental and clinical observation, we find ourselves confronted by a mass of material which, though valuable, does not yield us a final, dependable statement of fact. As regards the etiologic relationship of the enlarged thymus to the disease, it appears to me that it is plausible to assume that the enlargement of the thymus (as indeed the enlargement of the remaining lymphatic glands) is caused by and is therefore *secondary* to the surcharging of the blood with the products of an overactive thyroid gland. In support of this hypothesis we have only to recall that an undue amount of thyroid secretion is a real irritant or poison to the system and that the lymphatic tissues of the body usually assume the rôle of filters, for the protection of the blood stream against toxins, and undergo a compensatory hypertrophy in the performance of this protective function. The value of any statement in answer to the problem would be materially increased were we able to obtain an estimate of the percentage of persons not afflicted with exophthalmic goiter, yet possessing a thymus the size of which is greater than the accepted standard.

The Adrenal Theory.—Some observers hold that a deranged structure and function of the suprarenal glands is responsible for the Basedowian syndrome. In support of this view it is pointed out that the subject of Graves' disease commonly presents areas of pigmentation, which in some instances constitute a prominent element in the symptomatology. Moreover, it has been observed that symptoms of Addison's disease will occasionally precede, coexist with or follow those of the syndrome of Graves' disease.

Here the statements of W. B. Cannon (Bull. Johns Hopkins Hosp., 1916, XXVII) are suggestive: "The bodily changes accompanying strong emotions, such as fear and rage, are related to certain glands of internal secretion, especially the adrenals, and probably the thyroid. When infuriated a cat's pupils are dilated, hair stands erect, heart is accelerated, the activities of stomach and intestines inhibited, and muscular fatigue lessened. There is an increased liberation of sugar from the liver, an increase of circulating erythrocytes, and the coagulation time of the blood is decreased. These changes also occur in man. Fear and rage are emotions underlying the struggle for existence and the changes noted increase the efficacy of the organism for physical struggle. Most of the phenomena noted are due to increased circulating adrenin, the adrenal glands being stimulated by the sympathetic nervous system." This author believes that the reason organs disturbed during emotional stress are not disturbed at other times is that a high neuron threshold is interposed between the central nervous system and the visceral cells. This threshold is only crossed when great excitation is present in the central nervous system. In pathologic cases the threshold is lowered from great emotional experiences, and there is a frequent disturbance of these organs, causing dyspepsia, tachycardia, and glycosuria. Besides a routine function, the adrenals have an emergency function in times of great excitement. This is likewise true of the thyroid, its increased activity augmenting the metabolic processes and aiding the efficiency of the adrenin. (Endocrinology, Vol. I, 1917.)

In view of the occasional evidences of a combination of Addison's disease and exophthalmic goiter in the same patient, and in consideration of certain significant clinical and experimental circulatory phenomena and the fact that the administration of suprarenal extract is of signal benefit in a certain percentage of Basedow patients, the conclusion that the suprarenals play *some* rôle in the syndrome of Graves' disease seems justifiable.

The Parathyroid Theory.—The incrimination of the parathyroids as the causal agent in the production of exophthalmic goiter was suggested by the remarks of Gley. This observer based his views especially on the statement that the parathyroid tissues are almost identical with those of the thyroid, the former being an undeveloped or embryonic form of the latter, and that the tremor and many other symptoms indicate a primary parathyroid derangement. Though this theory found favor in the eyes of Jean Clunet and others, the vast majority of observers do not accept it seriously.

The Pituitary Theory.—In 1905, and again in 1911, Salmon pointed out that the Basedowian syndrome is produced by a derangement of function of the pituitary. He bases his deductions upon the following points:

1. Experimental thyroidectomy has, in a large number of cases, produced a hypertrophy of the pituitary, characterized microscopically by a picture of hyperfunctioning glandular cells (Lucien, Parisot and Thaon).

2. Pituitary extract exerts a vasoconstricting action on the thyroid, which is quite intense and durable.

3. There exist in literature several observations of syndromes of acromegaly associated with Graves' disease,

some of which were verified at autopsy by the discovery of hypertrophy or neoplasm of the pituitary.

4. Pituitary opotherapy has ameliorated a number of cases of Basedow's disease. Of 12 cases, Parisot has cured 2 and improved 8 with this treatment (Rénon and Delille; Parisot; Azam).

That Salmon's theory is more than mere speculation is exemplified by the statements made in the chapters on Physiology and Treatment. Hypertrophy or disease of the pituitary body is commonly seen in autopsies of cases of Graves' disease; moreover, there is accumulating evidence to convince one of the value of pituitary extract, especially the newer product "tethelin," in this disease.

The Gonad Theory.—It seems that in many cases of hyperthyroidism the organs of reproduction, especially in the female, are at fault. Roussy suggests that the ovary and thyroid react on each other. Absence or deficiency of thyroid is known to result in arrest of sexual development, as pointed out in the chapter on Physiology. It is also known that during puberty and menstruation the thyroid is in a physiologically hyperactive condition. Experiments of Hallion have proved that ovarian therapy causes vasodilatation within the thyroid gland. In some instances ovarian therapy has succeeded in ameliorating the symptoms of exophthalmic goiter. Vinay and others have pointed out that the Basedowian syndrome may appear after spontaneous or operative menopause. It must therefore be concluded that whatever relationship the thyroid bears to other organs, the relationship to the female genital tract is one of etiologic interest.

Hertzler reports 12 cases of pelvic disease in association with exophthalmic goiter, and says that relief of a pelvic lesion in certain cases is followed by amelioration of the thyroid symptoms. He further remarks that in certain instances it seems probable that the pelvic lesion stands in a causal relationship to the goiter.

T. B. Eastman reports 2 significant cases. In one with a fibrocystic ovary associated with enlargement of the thyroid gland, removal of the ovary and tube resulted in relief from the hyperthyroidism. In the second case, one suffering with dysmenorrhea and menorrhagia, with a normal pelvis and all the typical findings of hyperthyroidism, removal of a part of the thyroid gland relieved her menstrual as well as thyroid symptoms. He concludes that there is a close interrelationship between the ovaries and thyroid. Thyroid secretion and ovarian secretion do not supplement each other, they neutralize each other (Endocrinology, Vol. I, 1917).

The Moebius or Hyperthyroidism Theory.—According to Moebius (1886), Graves' disease is due primarily to disease of the thyroid gland, in which there is an excess of thyroid secretion thrown into the blood, causing the symptom-complex. This is supported by the following clinical facts:

(1) The condition is the direct antithesis of myxedema, in which there is a lack of thyroid substance in the blood.

(2) Partial reaction of the goiter or partial ligation of the blood supply causes at least a diminution of the symptoms.

(3) Most, if not all the symptoms of exophthalmic goiter, may be artificially produced by the oral administration of thyroid.

(4) Thyroid gland, administered to a subject of Graves' disease, aggravates the symptoms.

(5) Other theories fail to explain satisfactorily the causation of the syndrome.

Others have presented views modifying somewhat the essential views of Moebius. Gauthier (1885) believed exophthalmic goiter to be the result of thyroid insufficiency. Renaut (1888) in a thesis states that exophthalmic goiter is a toxic disease, possibly of infectious origin, resulting from the penetration into the venous system of thyroid secretion.

Wm. E. Greenfield states that the thyroid secretion is increased in quantity and altered in quality.

Lampe and Klose are of the opinion that the disease is due to a **dysthyroidism.**

Béclère, Pierre Marie and others concur with Moebius in stating the Basedowian syndrome to be the result of a hyperthyroidization of the body, basing this conclusion on the results of thyroid medication.

This conclusion is amply confirmed by Ballet and Enriquez who, in 1895, experimentally produced the Basedow syndrome by thyroid administration.

In criticism of the Moebius theory, an editorial in Endocrinology (Vol. II, No. 4,) states that: "One observation which is apparently well attested renders untenable the conception that Graves' disease is a simple hyperthyroidism. This observation is that the disease may exist simultaneously with hypothyroidism. Thyroid secretion can not be both augmented and depressed at the same time any more than can a physical body be simultaneously up and down. Various labored explanations of the paradox have been offered, but they have the defect of leaving the contrary fact still standing. Moreover, cases in which thyroid medication has proved beneficial in Graves' disease have been repeatedly described. The blood picture—a reduction of neutrophiles, lymphocytes, and mononuclear leucocytes—is the same in both Graves' disease and myxedema. It would seem, then, that there is some element in common in the etiology of both conditions."

N. W. Janney, from the result of his own work and a critical review of the literature, is also led to doubt the adequacy of the hyperthyroid theory of exophthalmic goiter. A tentative theory is put forward which assumes that the result of the premature discharge of a "hypothetical toxic intermediary product" would result in an impoverishment of the gland of the thyroid hormone. Such a theory would explain the fact that the thyroid tissues in Graves' disease are poor in iodine and especially in the Alpha-iodine proteins. The decreased production of the normal hormone due to this cause would tend to be accompanied or followed by signs of thyroid insufficiency. Thus the deficiency signs can be accounted for; also the concomitant occurrence of hypothyroid and hyperthyroid symptoms, and the tendency of exophthalmic goiter patients to develop myxedema.

No one can deny that despite one or the other theories the syndrome is due to an excess of thyroid hormone circulating in the blood. Now, thyroid hormone is elaborated by the thyroid gland. We are therefore forced to the conclusion that, in view of the other plausible theories, especially the pluriglandular views, and since the administration of thyroid extract in Basedow subjects aggravates the syndrome in nearly every case, the thyroid gland is made to elaborate and discharge a surplus of its secretion into the body tissues, which process is directly or indirectly instigated by one or more agencies elsewhere in the economy.

Pluriglandular Theories.—These are numerous and variable and lend themselves to considerable speculation. Stengel, Solomon Solis-Cohen and others firmly believe that the thyroid excess in the blood, through thyroid hyperfunction, is but an incident in the chain of events occurring in all the other glands, especially the endocrines of the body, all of which conspire to produce the syndrome. As observed in the chapter on Physiology and elsewhere, there are pathologic, clinical and therapeutic evidences to confirm the belief that the suprarenals, pituitary, parathyroids, ovaries, thymus, and even the pancreas and liver are interrelated in function with the thyroid, and in the event of a departure from the normal structure and function of one of these glands, the others are affected.

To exemplify: It has been observed that the thyroid and suprarenals, under certain conditions, stimulate each other; the thyroid and pancreas depress each other; the pancreas and suprarenals are also mutually inhibitory. A state of hyperfunction of the thyroid, then, will increase the activity of the suprarenals and depress that of the pancreas. The latter fact has even led to the supposition that a removal of part of the thyroid gland might ameliorate the symptoms of diabetes. This is seemingly confirmed by the experiments of Lorand, according to which the glycosuria of animals deprived of the pancreas disappeared when the thyroid was removed.

Roussy points out that the sympathetic is also implicated in this glandular interrelationship, in that adrenalin causes sympathetic excitation, and that the thyroid secretion excites the sympathetic and autonomous systems simultaneously. The researches of Eppinger and Hess are of value in connection with this phase of the question.

To conclude, it must be conceded that the *modus operandi* of the Basedowian syndrome is not simple but is one of the most difficult problems in medicine, necessitating continued painstaking clinical and laboratory investigation. The primary etiology of goiter, whether simple or exophthalmic, is never to be found in the thyroid gland itself. In other words, both simple and toxic goiters are secondary conditions dependent upon causes outside the thyroid gland.

CHAPTER V

SYMPTOMATOLOGY OF EXOPHTHALMIC GOITER

No morbid condition is as protean in its manifestations as is exophthalmic goiter. No mere outline can amply and faithfully describe any given case; no case corresponds in symptomatology to any given outline with more than relative accuracy. Moreover, the variations in the symptomatology from time to time in the same patient, especially in the early stages, and the accuracy with which a given case can mimic certain other better known conditions, add to the difficulty.

In this chapter we shall briefly survey the symptomatology of the following forms of the disease: 1. Acute Basedow's disease; 2. Chronic or Usual Type; 3. Basedow "Fruste"; 4. Secondary Basedow; 5. Artificial Basedow.

I. Acute Basedow's Disease

The rapid, acute, "abortive" type of Graves' disease is fortunately not often encountered. A case of J. H. Lloyd's quoted by J. M. Anders, proved fatal after an illness of three days. The course is rather malignant; there is marked, rapid loss of weight. The patient may lose one-half of the body weight within a few weeks. The most constant symptom is tachycardia, usually associated with distressing palpitation, and which may lead to arrhythmia. There is high blood pressure, occasionally fever and severe gastrointestinal symptoms with incessant vomiting and purging. The exophthalmos is marked, and at times there are cerebral symptoms leading to one of the various types of mental aberration. The patient may die in an attack of acute delirium, dementia, or from collapse due to the incessant nausea and vomiting. Finkle reports 4 cases of acute exophthalmic goiter whose most marked symptoms were tachycardia and rapid and excessive loss of weight. He emphasizes the fact that in no other disease does the patient lose so rapidly in weight—in a case of Schlessinger's 122 pounds in eleven weeks, in one of his own patients 48 pounds in a few days, and in another 110 pounds in a few months. There was no enlargement of the thyroid in 2 cases and none in the beginning in another case in which later a large goiter developed. The tachycardia was constant and in some became a perpetual irregular arrhythmia; the blood-pressure also ran up extremely high and in one of the cases has persisted high although there was nothing to indicate kidney disease. Fever of a remittent type was occasionally observed, especially in a case accompanied by motor disturbances resembling the severest type of chorea, persisting for some time after subsidence of the other symptoms. In addition to the clonic spasms in this case there was also contracture of the hands, suggesting tetany. The onset of trouble in one case simulated severe gastrointestinal poisoning. All the cases improved in time to a condition which amounts to a clinical cure. Treatment was hygienic-dietetic with complete rest, kept up for a long time, supplemented later by mild hydrotherapy.

An acute exacerbation of the usual chronic form of the disease resembling in clinical aspects an acute Basedow, occasionally follows a thyroidectomy and is often seen by thyroid surgeons. This is a common cause of postoperative death. During the course of the operation or immediately after, often as the patient comes out of the anesthetic, he is seen to undergo a state of great excitation with marked delirium, exaggerated tremor, extreme anxiety, drenching perspiration, and at times, hallucinations and mania. The pulse mounts up to 180, 190 or even 200, soon becoming feeble and impalpable; there is high fever, vomiting and incontinence of urine and feces, usually terminating in fatal collapse within a day or two. Rarely a case of this sort recovers. The cause of acute postoperative hyperthyroidism is variously given by different clinicians. Kocher believes it due to the general anesthesia; Crile to shock. My own impression is that this crisis is merely the result of surgical interference with a vital organ. All meddling with vital organs, whether it be the brain, the heart, pituitary or the thyroid is apt to lead to a fatal crisis of some character, the exact *modus operandi* of which we do not understand in the present stage of our knowledge.

II. The Chronic or Usual Type

A subject of the chronic or usual type of the disease may appear in the doctor's office complaining merely of muscular weakness of a few weeks' duration, with progressive loss of weight; or the chief complaints may be occasional palpitation, nervousness, and insomnia; or in some instances the dominant subjective feature may be frequent diurnal and nocturnal micturition which causes the subject to suspect diabetes or Bright's disease. Occasionally marked sweating, especially at night, will become so regular and exhausting, that the patient will fear the existence of tuberculosis and will consult the physician with this diagnosis in view. Indeed, the onset of this disease may vary so greatly from the classical syndrome that only too often the patient, and even the general practitioner will diagnose the case under such headings as "nervousness," neurasthenia, "run down system," nervous dyspepsia, anemia, pulmonary tuberculosis, and even diabetes mellitus.

The **tachycardia** is a more or less constant and conspicuous feature of the disease and, in combination with subjective precordial distress, may precede for a variable period of time the other cardinal symptoms. This heart hurry (of 90 to 140 or more per minute) and palpitation with dyspnea are a combination of symptoms for which the subject most often seeks relief.

Goiter may be absent for a while or appear in variable degree with the onset of other cardinal symptoms or some time afterward. Occasionally, the thyroid gland maintains its normal size during the course of the disease. The increase in size of the thyroid is never excessive in true primary Basedow's disease. In a small percentage of cases the patient becomes aware of the existence of the affection only after discovering that the clothing about the neck becomes too tight.

Exophthalmos or protrusion of the eyeballs, usually bilateral, is present in the great majority of cases, and as a rule, occurs at a variable time following the appearance of other symptoms significant of the disease. The degree of exophthalmos varies with the severity of the case and in the same individual at different times. Associated with this symptom, the Von Graefe, Stellwag, Moebius, Dalrymple and other eye signs may be observed. These are later to be described.

Tremor is present as a rule, and often exists as an early sign. These are fine, involuntary, and obtained by having the patient extend the arms and stretch the fingers apart. Along with muscular tremors may be observed psychical disturbances of varying degree, viz., insomnia, mental depression, neurasthenia, depressive periods, melancholia, and rarely one of the psychoses.

One of the most prominent manifestations of hyperthyroidism is the extreme susceptibility of the patient to fatigue. He or she "feels weak," "has no ambition," the thigh and calf muscles feel as though they have been inactive for months, there is no physical or mental drive to action, and the patient feels "all in." Often these flexors and extensors feel as though they have been beaten; they are sore, demand rest, and when the patient endeavors to recline, he discovers that his hands and feet tremble. In brief, though the patient seeks repose, he finds to his dismay that complete rest is impossible. It has often been seen that most of the symptoms of hyperthyroidism are aggravated by lying down, and that these patients, far from feeling refreshed by a night in bed, arise in the morning feeling worse than ever.

The marked bodily wasting is not only an early symptom of hyperthyroidism, but is a conspicuous accompaniment of the other manifestations during the entire course of the disease. This marked wasting is probably due to the well known oxidizing quality of thyroid secretion, first destroying fatty, then albuminous tissue, and is probably an action analogous to that claimed for it in the destruction of albuminous toxins of the intestines. The increased metabolic rate in thyroid toxemia may vary widely and does not depend upon the size of the goiter, but upon the degree of thyroid toxemia. In some cases the rate may reach 75 or even 100 per cent above normal. Thus, a patient formerly strong and robust becomes within a few months or a year or two, a weak, tired creature often even more emaciated than if she were affected with an advanced stage of diabetes mellitus or phthisis.

Certain other signs and symptoms referable to the circulatory, nervous, gastrointestinal, respiratory, cutaneous and genitourinary systems will be described under separate headings.

Vagotonia and **Sympatheticotonia.**—In Graves' disease we may meet with symptoms indicating a predominance of a stimulation of the vagus system on the one hand, or a prominence of symptoms due to stimulation of the sympathetic on the other. In other words, every subject of progressive hyperthyroidism will sooner or later present symptoms of vagotonia, of sympatheticotonia, or a combination of the two. The studies in visceral neurology by Pottenger and the observations of Eppinger and Hess, Coenan and others have added materially in a partial elucidation of the subject. The remarks of J. H. Smith are of service: "By vagotonia is meant the clinical appearance of chronic or recurrent symptoms recognized as manifestations of overactivity of the vagus system.

"The two parts of the vegetative system, the sympathetic and vagus, exert a constant balance on one another.

The normal excitant of the sympathetic is adrenalin; that of the vagal system is not known.

"The fundamental fact in anaphylaxis is proteolysis. The vagus system and muscles supplied by it are chiefly influenced. Anaphylaxis manifests itself through vagus irritation.

"Toxic influences, especially anaphylatoxins, may be considered as underlying the vagotonic state. Definite proof exists of the anaphylactic nature of certain cases presenting vagotonic manifestations, viz., parasitic infestations, food idiosyncrasies, asthma and hay fever.

"In the interpretation of vagotonic symptoms without apparent cause, two toxic factors are among the possibilities—ductless gland disturbances and chronic bacterial infection.

"Two types of thyrotoxicosis are mentioned, the division following the line of physiologic antagonism between the vagus and sympathetic systems. In the vagotonic cases there is present a vago-irritant toxin; in these cases there is probably a preponderant influence of the thymus.

"Increased sugar tolerance is a phenomenon connected with abnormal conditions of the ductless glands. This tolerance, seen in vagotonics generally, is suggestive of a causal relation of the ductless glands to the symptom-complex vagotonia.

"In the treatment of vagotonic symptoms adrenalin gives good results; also in urticaria and sometimes in bronchial asthma."

The division of the symptomatology of Graves' disease by Eppinger and Hess as to whether vagotonia or sympatheticotonia predominates, are concisely stated:

(a) Characteristics of the vagotonic type are: 1, relatively slight increase in pulse rate; 2, subjective cardiac symptoms; 3, marked Von Graefe's sign; 4, wide lid slits; 5, very moderate exophthalmos; 6, marked epiphora; 7, excessive sweating; 8, profuse diarrhea; 9, gastric hyperacidity; 10, eosinophilia; 11, disturbance in respiratory rhythm; and 12, absence of alimentary glycosuria.

(b) Characteristic of the sympatheticotonic type are: 1, marked exophthalmos; 2, epinephrin mydriasis; 3, Moebius' sign; 4, frequently dry eye; 5, a high degree of tachycardia with subjective cardiac symptoms; 6, no sweating; 7, no diarrhea; 8, falling out of hair; 9, rise in temperature; 10, absence of eosinophilia; and 11, alimentary glycosuria.

Pottenger, in commenting upon this division, remarks that "in these two types of Graves' disease it should be noted that the vagotonic type shows a general widespread parasympathetic stimulation, while the sympatheticotonic type shows most marked symptoms on that part of the sympathetic system whose motor cells lie in the cervical ganglia. The two noticeable exceptions to the last statement are slight rise in temperature and alimentary glycosuria which, if due to sympathetic stimulation or increased adrenal secretion, are a result of general and not a local action. The adrenals are stimulated by thyroid secretion."

In view of the existence of inconsistencies in the above classification, when an attempt is made to check up, as it were, these phenomena with those presented by the average case of exophthalmic goiter, further study of the functions of the nervous system and the endocrine organs is necessary before we can utilize these data clinically with any degree of precision and assurance.

Hyperthyroidism with Hypothyroidism are sometimes seen in the same patient, indicating instability of extreme degree. Leopold Levi reports the case of a woman aged thirty-three, 164 cm. tall, and weighing but 40 kg., who exhibited alternately, and at times even in conjunction, pronounced symptoms of hypothyroidea and hyperthyroidea. Under the influence of the nocturnal reduction in temperature, the patient passed into a condition verging on myxedema, while in the postmenstrual period her condition suggested Graves' disease. Intervening between periods of hypothyroidea and hyperthyroidea were normal periods, the latter amounting, however, only to a few days in each month. The instability witnessed is ascribed to variations in the circulation through the thyroid, inducing alternate states of inertia and overactivity in its function. A partial hyperemia of the gland awakens a paroxysmal hyperthyroidea upon a substratum of hypothyroidea. The patient also presented evidences of lowered ovarian activity and of adrenal instability. She showed all the earmarks of a lack of nervous equilibrium and of angioneurosis—in brief, a state of neuroendocrinic instability in which participated to a predominant degree instability of the thyroid itself.

An editorial in the Journal of the A. M. A. (Dec. 14, 1918) makes the following comment on this perplexing problem:

"Janney has proposed to discard the seemingly inadequate hyperthyroid explanation and substitute for it 'dysfunction' of the thyroid to explain the phenomena. In the light of this we can now understand that some of the symptoms of exophthalmic goiter—the thyroid enlargement, cutaneous symptoms, scleroma, osseous changes, and special metabolic manifestations, such as hypoglycemia—are identical with those of a hypothyroidism attributable to a poorly functioning gland. They are truly symptoms of thyroid deficiency which have usually been disregarded in the symptomatology. The more familiar manifestations—psychic stimulation, tremor, tachycardia, increased basal metabolism, etc.—are toxic symptoms which Janney assigns to the liberation of intermediate products of poisonous nature, perhaps owing to the incapacity of the glands to produce the normal thyroid hormone. In exophthalmic goiter, then, a toxic substance is circulating in the system. With a defective endocrine secretory function postulated, it becomes evident how hypothyroid and toxic symptoms may be discovered concomitantly.

"With this tentative explanation it becomes clear, furthermore, how clinical improvement may follow suitable—

not excessive—thyroid dosage in some cases, particularly when the thyroid deficiency is the etiologically prominent though perhaps not symptomatically conspicuous factor. It is also evident, on the other hand, that the introduction of a normal hormone from without to a dysfunctioning as well as underfunctioning endocrine organ 'may not necessarily lead to a cessation of the chemopathologic processes causing the toxic symptoms' of exophthalmic goiter. Probably thyroid treatment of these toxic cases is inadvisable; but when the deficiency symptoms appear, thyroid therapy may actually be indicated, despite the objection which the still current hyperthyroid hypothesis interposes. Is it too much to expect that the stimulus of Janney's recently expressed views will lead to new clinical and therapeutic investigations untrammeled by the handicap of preconceived notions?"

Leopold Levi and H. de Rothschild, in an interesting treatise, also point out that hyperthyroidism is often succeeded by hypothyroidism, and that the two conditions may coexist in the same subject, implying that this is due to thyroid instability or dysthyroidism.

Cases of this sort seem to flout not only most of the clear cut etiologic theories of Graves' disease, but also render the diagnosis more difficult than ever. On second thought, however, an explanation of the cause of this contradictory combination is not difficult to find. Although some observers believe that in *every* case of hyperthyroidism there is a degree of hypothyroidism, this is probably not so in the early and moderately advanced stages of the disease. The most probable explanation of the situation is this: Marked persistent stimulation of any organ leads to depression of function. As in the case of the heart in exophthalmic goiter in which the tachycardia brings on hypertrophy to be followed by dilatation and heart failure, so it is with the function of the thyroid in principle. The hyperfunction of this organ goes on for months, or in the absence of accidents, for a year or two until finally the thyroid, "tired" of overwork, slows down, and the symptoms are ameliorated. If this retardation of function does not continue to below the normal point, we have a natural cure, and the patient has fortunately obtained a spontaneous recovery from the syndrome. In many instances, however, this recession from hyperfunction is due to depression from a *degeneration* of the thyroid substance which soon spreads throughout the gland. Thus, in the progress of events after the normal degree of secretion is reached and the relatives and friends have rejoicingly observed a return to normal of all bodily function, the patient begins to gain more weight than usual, the features gradually become stupid and expressionless, the skin becomes dry, pale, and doughy, speech is slow and monotonous, cerebration is tardy, and somnolence is continuous. We have here a case of hypothyroidism or myxedema secondary to a siege of hyperthyroidism. It is not difficult to conceive of a sort of transitional stage in the above mentioned process during which symptoms of hyper- and hypothyroidism coexist, or even a lapse of time during which hours of apparent manifestations of hyperthyroidism alternate with like periods of hypothyroidism or vice versa.

In addition to the tachycardia, enlarged thyroid, exophthalmos and tremor which constitute the classical cardinal symptoms, certain miscellaneous signs and symptoms referable to the cutaneous, gastrointestinal, respiratory, genitourinary tracts and elsewhere are commonly observed and will be described under their respective headings.

III. Basedow "Fruste"

Just as in most morbid conditions there is an incomplete stage in which the manifestations are indistinct, vague, doubtful, and at times misleading, so in hyperthyroidism there is often a variable period of time during which the affection may be considered in the incipient, or, as it were, "embryonic" stage. Also, just as in the study of tuberculosis, diabetes and other affections we note that there are hundreds or thousands of individuals affected, but who are not aware of the same and go about their respective duties apparently unhampered by their affliction, so do we find latent cases of hyperthyroidism in which the subjective symptomatology is not quite urgent enough to force the patient to seek medical attention. These borderline cases, instances in which the diagnosis is uncertain, appearing now as neurasthenia, again as hysteria, here as nervous indigestion, there as "nervous breakdown," are to be classified as "light" Basedow or pre-Basedow cases or *formes frustes.*

These early or pre-Basedowian forms of hyperthyroidism may be further subdivided genetically into:

(*a*) The early or incipient stage of the usual progressive form of exophthalmic goiter—the stage of formation.

(*b*) The very mild form which may not progress to a typical development of exophthalmic goiter, all things being equal.

(*c*) Hyperfunction of the thyroid existing from early childhood and probably inherited.

(*d*) Secondary *forme fruste* depending upon changes in thyroid function instigated by the presence of an old nontoxic goiter or an infection of the thyroid.

Clinically, however, if not identical, the above types have many things in common, and the diagnosis is made by exclusion and only after careful study of each subjective and objective detail. For example, a young girl during the adolescent stage, often during attendance at college, begins to experience daily sensations of heat, and there arises a tendency to diarrhea. Sleep becomes restless, there is some loss of weight, she becomes irritable and lachrymose on the slightest provocation. There may be a slight fullness of the thyroid which is more noticable during menstruation, some palpitation, and the eyes are large and brilliant. Such an individual is frequently at the head of her class, occasionally with evidences of mental precocity. These symptoms may disappear without treatment within several months or a year, but more often they progress toward the development of a typical clinical picture of exophthalmic goiter. Under careful *nonoperative* treatment, however, especially with the complete cooperation of the patient and her relatives, such a case invariably recovers within a few months.

Again, under the stress of business pressure, a young man, having deprived himself of all recreation for a protracted period, begins to suffer with indigestion. He applies for treatment but his case is refractory to ordinary therapeutic measures, and within a short time not only are his subjective symptoms intensified, but he finds that he can not sleep and feels so irritable and restless that he fears he is losing his reason. His heart feels rather uncomfortable especially after eating, he is somewhat "short of breath" and is losing weight rapidly, though eating as much as usual. Finding that his collars are becoming a little tight, he soon discovers that his neck is somewhat full in front and hurries to advise his physician of the fact. Physical examination reveals a slightly hyperplastic thyroid, tachycardia, and perhaps a tremor of two or three fingers. A patient, persevering medical adviser will cure this case within less time than the probable previous duration of the affection.

Lian states that it is a delicate question to decide whether a subject, having palpitation and tachycardia, is a subject of an abortive form of Graves' disease. In the absence of a satisfactory biologic test to settle the question, we must depend on resources of some sort to differentiate between this and other forms of tachycardia, among which are paroxysmal tachycardia and many organic diseases, whether cardiac, renal, tuberculous, etc. He points out a significance of a new symptom—hyperesthesia over the thyroid region. This the author has noted in some 10 cases and his attention was attracted to it as a result of palpation of the thyroid for enlargement. In three of these there was enough outside evidence to make the diagnosis, but in the balance it is doubtful if any diagnosis could be made unless the value of this sign is acknowledged. This hyperesthesia is not of the type which one would ordinarily have in mind, but an increased sensitiveness to pain. Slight manipulations call forth a grimace of discomfort. In the typical case this area is limited to the gland. That the sign is a new one seems evident from the frequency of the statement that the goiter in this affection is insensitive. The sensitiveness is in all probability due directly to an increase in tension of the enlarging gland. The author recommends that in routine examination of the thyroid in obscure affections particular attention should be paid to undue sensitiveness of the organ.

It may be emphasized that a persistent nervousness, tachycardia, and hyperesthesia over the thyroid are almost constantly present and should assist in determining the existence of thyroid hyperactivity. The Goetsch adrenalin test and a blood examination should not be omitted.

With respect to the congenital form of the disease, Sainton and Delherm (quoted by Roussy) have described a form of hyperthyroidism which is a hyperesthesia or a natural hyperexcitability peculiar to women and manifests itself under the effect of any emotional trouble whatever by slight exophthalmos with peculiar brightness of the eyes, swelling of the neck, frequency of heart beats, and a state of light tremor. "Thus Stern has attempted to isolate a type of the disease called 'Basedowides.' These are persons with hereditary nervous predisposition and in whom towards the age of twenty years appeared a Basedowian syndrome somewhat masked: palpitations with pain, small goiter soft or resisting, with colloid nodosities, but causing a very keen embarrassment, spasmodic dyspnea, tremor, rapid pulse, but under 120. These patients are never cured, but on the other hand never become true Basedowites. According to Falta, on the contrary, this form predisposes to the Basedow."

IV. Secondary Basedow

Secondary Basedow or "Basedowified" goiters differ from the primary or hyperplastic type in that they are the result of changes instigated in the thyroid gland by other morbid conditions of the organ. Though an acute infection, tuberculosis, syphilis, and even malignant disease of the gland may in their respective courses initiate this secondary change, in the great majority of cases it follows as an intercurrent condition during the existence of a simple or nontoxic goiter, often occurring as the result of an exciting cause, as shock, worry, an attack of acute illness, prolonged physical or mental strain, traumatism to the neck, and the like. Occasionally, the hyperplastic process seems to arise without any exciting factor.

The symptoms occur some years after the appearance of the simple goiter. In this connection it is interesting to note Plummer's observations: "Patients coming under observation with nonhyperplastic toxic goiter give a history of having first noted the goiter at the average age of 22 years, and the evidence of intoxication at the average of 36.5 years. The corresponding ages for hyperplastic goiter are, respectively, 32 and 32.9 years. That nonhyperplastic goiter is noted ten years earlier in life than hyperplastic goiter, that fourteen and one-half years elapse between the appearance of nonhyperplastic goiter and the development of notable toxic symptoms, and that the constitutional symptoms were noted but a few months (between ten and eleven) later than the goiter in the patients affected with hyperplastic thyroid, is alone sufficient to show that we are dealing with at least two distinct pathologic and clinical groups. That one is not the sequence of the other is self-evident."

The syndrome of symptoms in secondary Basedow develops more insidiously than in the primary form and is less severe. A simple goiter may gradually become slightly tender and the patient may present a degree of tachycardia;

again a slight unilateral or bilateral exophthalmos may assert itself without any other manifestations of Graves' disease; or, the tremor may be the only accompanying feature for a long time. It is only occasionally that a thyroid gland of this type will assume a sufficient degree of increased function to approximate in symptomatology the clinical picture of a primary thyroid hyperplasia. This, however, is not true of the circulatory phenomena. In many instances the patient is found suffering with pressure symptoms because of the superimposition of all the signs and symptoms of the Kocher or Kraus "goiter heart." Pierre Marie emphasizes the importance of the intense paroxysms of dyspnea occurring especially at night, and marked sialorrhea in cases of this sort.

V. Artificial Basedow

Under this heading we include the untoward symptoms arising from the ingestion of thyroid extract and of iodine or the iodides. In both instances a special idiosyncrasy or susceptibility of the individual is to be presupposed, especially when the dosage of these substances was not excessive.

The administration of thyroid extract is in all cases fraught with a degree of danger unless taken in small doses at first and the patient is carefully observed at short intervals by the attending physician. Under these circumstances only can harmful results be avoided and the proper therapeutic effects obtained in cases in which thyroid is indicated. Most instances of artificial thyroid intoxication or thyroid toxemia through ingestion of the gland are due to the ignorance of the patient, which fact is occasionally a reflection upon the physician because of his neglect to warn his patient of the potency of the drug and the possibility of harm from its unguided use. Thus a subject of obesity, having been administered thyroid tablets for a while, will discontinue her visits to the physician, and finding that the "medicine" has yielded good results, will have her prescription renewed indefinitely. Sooner or later, the obesity, to be sure, is more or less overcome, but the patient finds herself nervous and fidgety, unable to sleep, perspiring profusely and altogether changed in many ways. A visit to her physician reveals the fact that she is suffering from the *fruste* or perhaps a well-developed syndrome of thyroid toxemia. Occasionally, this process of hyperthyroidization through thyroid ingestion is seen in persons to whom this drug was given for hypothyroidism primarily, so that here, too, care must be taken in warning the patient not to absent himself from the doctor's office in order that just so much and no more of the drug may be taken.

More rarely, the iodine products are capable of producing symptoms resembling hyperthyroidism from the early or *fruste* form to a well-developed type in degree. Here also, it is plausible to assume a marked idiosyncrasy to iodine, a predisposition to hyperthyroidism or both, in the individual in question. This "Iodine Basedow," so called, in exceptional instances may develop even from the local use of tincture of iodine. At first there are observed in varying degree the classical symptoms of iodism, viz.: coryza, evidences of gastrointestinal catarrh, bronchial catarrh, lachrymation, conjunctivitis, salivation and the typical skin eruptions. Sooner or later there is a development of palpitation, tachycardia, nervous irritability, tenderness over the thyroid gland, and other evidences of hyperthyroidism which in extreme cases develop into the typical syndrome of Graves' disease.

The discussion in greater detail of the symptoms of Graves' disease will now follow.

The Circulatory System in Exophthalmic Goiter*

The circulatory phenomena are not only the most important but also the most constant to be found in exophthalmic goiter. There is no Graves' disease without circulatory evidences; at least tachycardia is pathognomonic of the disease. The patient may present an apparently normal thyroid; there may be little or no tremor; even exophthalmos may have a doubtful existence; but a constant, rapidly acting heart, the rate of which is 90 to 200 per minute, day and night, awake or asleep, during activity or rest, usually associated with some precordial distress and dyspnea not traceable to a febrile condition, chronic poisoning from endogenous or exogenous matter (tea, coffee, alcohol, tobacco, iodism, intestinal or uremic toxins, endocarditis, etc..) is an almost positive indication of the surcharging of the blood with thyroid substance, either manufactured by the patient's own thyroid or ingested in the form of thyroid extract. It is the circulatory system which suffers most from the results of hyperthyroidism. It is the heart which ultimately determines the course and prognosis of the disease; its collapse is usually the direct cause of death from Graves' disease.

---

*"The Circulatory System in Exophthalmic Goiter" appeared as an article, in slightly modified form, in International Clinics (J. B. Lippincott Co.) Vol. I, Series 29, 1919.

In this discussion we shall divide the subject as follows:

CIRCULATORY PHENOMENA IN EXOPHTHALMIC GOITER

- (*A*) HEART
  - 1. Subjective
    - (*a*) Palpitation
    - (*b*) Anginoid pains
    - (*c*) Dyspnea
  - 2. Objective
    - (*a*) Tachycardia and differential diagnosis
    - (*b*) Physical examination
- (*B*) VESSELS
  - 1. Subjective
    - (*a*) Neck
      - (i) Throbbing sensation
      - (ii) Pressure symptoms
    - (*b*) Elsewhere—Throbbing sensations in large vessels
  - 2. Objective
    - (*a*) Neck—Physical examination
    - (*b*) Elsewhere
      - (i) Throbbing arteries
      - (ii) Pulse
      - (iii) Capillary pulse
      - (iv) Dermographia
      - (v) Blood pressure
- (*C*) BLOOD
  - 1. Subjective—Weakness of secondary anemia in advanced cases
  - 2. Objective—Blood findings

(A) Heart

The subject of *goiter heart* may here be mentioned, though it is questionable whether the matter really deserves clinical classification other than the consideration under exophthalmic goiter, since it concerns the simple more than the toxic goiters. Rose's goiter heart is due to mechanical impairment or injury of the thoracic veins, giving rise to cardiac hypertrophy and dilatation, and later, myocardial degeneration. Kocher's goiter heart is produced by respiratory embarrassment and dyspnea because of the tendency of the goiter to become intrathoracic in type. It is therefore seen that the "goiter hearts" of Rose and Kocher are largely the result of mechanical compression on the veins and often also the nerves of the chest by a nontoxic goiter. These symptoms usually occur some years after the onset of the goiter. The patient begins to complain of gradually increasing shortness of breath, there is cyanosis, dizziness, vertigo, alteration of voice, tinnitus aurium, and epistaxis. Palpitation becomes marked, and with the occurrence of cardiac dilatation, edema and anasarca gradually supervene.

The heart characteristic of toxic goiter, (thyrotoxic goiter) is the heart of exophthalmic goiter, but may occur during the course of simple goiter when the latter becomes "Basedowified." It is occasionally discovered that a heart is suffering from both thyroid toxemia and mechanical interference at the same time, as when the thyroid of a subject of the Rose and Kocher "goiter heart" begins to become "Basedowified." As we are here concerned primarily with the Basedowian or thyrotoxic heart, let us proceed:

1. In exophthalmic goiter the subjective symptoms referable to the heart are probably the first to manifest themselves, causing the patient to apply to a physician for treatment.

(*a*) Palpitation is defined by J. M. Anders as "a more or less rapid action of the heart that is perceptible to the patient and usually accompanied by an increased force of the cardiac contractions or a disturbance of the rhythm including extrasystole, and often also by precordial distress, anxiety and dyspnea.'' Under ordinary circumstances we ought not to be aware of the function of the heart; it goes on beating, and we go about our affairs with no more cognizance of it than our awareness of the continued activity of the stomach, liver, pancreas, and other organs of the body. An organ which makes its function known to us by attracting our attention is one whose function is abnormal. The palpitation of exophthalmic goiter at first occurring to a slight degree and only on exertion or mental excitation, soon begins so to trouble the patient as to occasion extreme restlessness, nervousness, and insomnia. Sooner or later, it becomes constant, with extreme exacerbations during exercise and emotion. The symptom is particularly marked when lying on the left side so that these patients find sleep difficult excepting when lying on the opposite side or on the back. Nervousness is an almost constant accompaniment of palpitation, and there is a question in my mind whether this occurs independently of it, whether the latter precedes and causes the nervousness, or conversely, whether the nervous phenomena cause the palpitation. Is this another vicious circle occurring in the syndrome of hyperthyroidism? This question still awaits solution. A further characteristic of the palpitation is the fact that the severity of this symptom does not depend on the degree of tachycardia; a mild degree of tachycardia may coexist with marked palpitation, and on the other hand, a patient with a severe tachycardia may not complain very much of palpitation.

(*b*) Anginoid precordial pains, so severe as to resemble angina pectoris and occasion a degree of unconsciousness of variable duration, may occur when the subjective heart symptoms are particularly marked. Although a thyrotoxic heart may occasionally evince signs of genuine angina pectoris, fortunately these symptoms are rare, occurring chiefly in male subjects with a history of syphilitic infection, alcoholism, or chronic nicotine poisoning.

(*c*) Dyspnea resulting from cardiac excitation frequently reaches the point of extreme shortness of breath on going upstairs and after some slight exertion, often giving rise to a suspicion of some pulmonary disease. Frequently this complaint, plus the finding of a diminished respiratory expansion in the presence of the characteristic loss in weight and strength may lead the general practitioner to a diagnosis of pulmonary tuberculosis.

2. Objective phenomena of the heart in exophthalmic goiter are extremely important.

(*a*) Tachycardia depends largely on the severity of the disease, its duration, and the condition of the heart before its onset, the heart rate varying from 90 to 200 per minute. Tachycardia is probably caused by stimulation (through thyroid intoxication) of the accelerator nerves of the heart coming from the sympathetic, and to a lesser extent of the inhibitory fibers of the vagus. The diminished peripheral vascular tonus and the increased tissue metabolism also contribute to the process. The acceleratory stimulation being far in excess of that of the inhibitory, causes the heart to bound away at an enormous rate. Investigators assert that the stimulation of the vagus, causing universal peripheral vascular dilatation, occasions increased thyroid vascularity and an increased formation of thyroid substance; the latter, thrown into the blood, stimulates the vagus; thus another vicious circle is formed.

The distinctive feature of the rapidly acting heart in exophthalmic goiter is its constancy. It is well to remember that under normal conditions in infancy and childhood the pulse rate is higher than in adult life; in the baby at birth, it is 140; at the age of three, the pulse is 90 to 100; in adult males it is 68 to 72; in females, 72 to 76 per minute. In hyperthyroidism the pulse rate may be even greater in frequency than that of the infant; in the early stages, it is 90 to 110; in moderately advanced cases it may reach 160; and in markedly advanced conditions (not infrequently associated with auricular fibrillation) a rate of 200 may be reached especially during physical or mental excitement. The tachycardia is constant even during sleep. It is useful at this point to differentiate the tachycardia of hyperthyroidism from certain other conditions giving rise to rapid heart action, among which we may mention the following:

Emotional states (anger, fright, terror, joy, anticipation) are associated with an increased pulse rate. The nervous patient on entering the doctor's office often presents a pulse of double its normal rate. Accordingly, the physician while taking the pulse will engage the patient in conversation for some minutes in order to distract the subject's mind from himself. These instances of increased pulse rapidity assume the normal on the disappearance of the cause.

Hysteria and neurasthenia very often present a rapid pulse, but a careful history of the case and the results of physical examination will soon reveal the cause. Here the pulse condition is transitory, returning to normal after a short time.

The so-called "shell shock" commonly seen in the army and navy, characterized by an irritable heart action, can not easily be differentiated from hyperthyroidism. This topic is discussed in detail in the chapter on shell shock.

Occasionally a doctor will meet a case in which the heart rate is approximately 90 per minute, but which, in the absence of discoverable causes and subjective discomfort, forces him to conclude that this is a congenital peculiarity of the individual.

The febrile diseases are always accompanied by an increased pulse rate amounting approximately to ten beats for each degree above normal temperature, depending upon the type of the disease from which the patient is suffering. A careful history and examination of the patient will lead to the proper conclusion.

The various toxemias, eminently lead, arsenic, mercury, phosphorous, tea, coffee, alcohol, (tobacco has been mentioned), are all capable of giving rise to more or less increased heart rate. In this category must be included the endogenous toxemias from the intestines, liver, and renal insufficiency. The differentiation from the tachycardia of exophthalmic goiter is easily made.

The essential anemias, such as pernicious anemia, chlorosis, and leukemia, and also debility from wasting disease, may occasion a rapid heart rate for a variable length of time, which is slowed down by rest. In the recent epidemic of Spanish Influenza many instances of persistent feeble rapid pulse lasting for weeks following the acute manifestations have been observed. This is due largely to a too early resumption of daily duties.

Paroxysmal tachycardia occurs at intervals; the pulse rate is much more rapid than in Graves' disease (usually about 200 or more a minute); there is a sense of extreme cardiac discomfort and of impending danger, with marked prostration and often syncope. Here the heart rate suddenly becomes normal within from a few hours to several days, and there are no evidences of hyperthyroidism.

The rapid heart action of chronic endocarditis is easily differentiated by the history and the physical examination revealing the presence of organic heart lesions. Acute endocarditis with its sudden, marked febrile manifestations is easily differentiated by the clinical history and a physical examination.

Among certain miscellaneous conditions which give rise to a rapid heart are surgical shock and hemorrhage, diseases of the central or peripheral nervous system, pressure due to cysts, tumors, abscesses, aneurysm, and certain other chronic diseases, as a latent tuberculous focus, Addison's disease, arthritis deformans, and locomotor ataxia. All these may be diagnosed with a reasonable amount of care and need not detain us here.

(*b*) The physical examination of a subject of hyperthyroidism, in revealing to an extent a condition of the myocardium, will give us some information concerning the course and the prognosis of the disease. *Inspection* in mild cases presents an intensification and diffusion of the heart beat, so that the apical area is greatly increased in size. As the condition advances, the heart bounds in the chest; the entire thoracic region seems to shake by the intensity of the heart beats. This also occurs when the patient is quiet or is in a sitting posture. So intense is the action of the heart that some observers claim to have heard the heart beats at a distance of 3 or 4 feet from the patient's chest in severe cases. Advanced cases with marked hypertrophic dilatation of the myocardium will present a diffusion of its apex beat, even into the left axillary space. *Palpation* presents a thrill over the cardiac area in moderately advanced cases and especially in late cases in the presence of mitral regurgitation, in which instance the palpating hand applied over the precordial area will be raised with each systole. *Percussion* at first presents nothing abnormal. Later there are evidences of beginning enlargement of the heart, and finally as hypertrophy and dilatation supervene and become marked, the area of the heart is extended downward and to the left until the apex reaches the sixth or seventh interspace at or near the anterior axillary line. Incidentally, careful percussion over the upper part of the sternum may reveal the presence of an enlarged thymus gland. The increase in size of the heart and of the thymus may easily be confirmed by an x-ray examination. The causes of cardiac dilatation are myocardial poisoning by thyroid substance resulting in cellular degeneration, and exhaustion of the heart through increased activity. *Auscultation* at first reveals nothing of importance excepting a more forcible and accelerated apex beat and possibly a hemic murmur over the base. Later, the dilatation of the cardiac chambers through the exhaustion of the heart muscle gives rise to a weakening of the heart beat and finally a mitral systolic murmur heard over the apex and transmitted into the left axillary space. As dilatation progresses, a tricuspid and an aortic murmur are apt to develop, leading finally to general anasarca and heart failure. During the early and moderately advanced stages of the disease, the second pulmonic sound is apt to be accentuated. During an oncoming dangerous dilatation with impending loss of compensation, a state of cardiac arrhythmia often occurs, serving as a warning of imminent danger.

White and Aub state that auricular fibrillation, including the paroxysmal type, is not uncommon in hyperthyroidism as shown in a series of six out of 47 cases of hyperthyroidism (13 per cent). Paroxysmal auricular flutter was seen in one case. Tachycardia, frequently hypertension and frequent tremor while at rest occurred in these cases of hyperthyroidism, although not always parallel to the total metabolism.

The "gallop rhythm" (Salhi) is an interesting phase of the cardiac physical signs and is a diastolic phenomenon. It is a triple rhythm heard over the entire heart. The tones follow at nearly equal intervals. The second of the three sounds is ordinarily accentuated over the apex and the third over the great vessels. The extra tone occurs during diastole just before the normal first tone and differs from the presystolic tone of mitral stenosis in that it is generally heard all over the heart. It is probably due to the excessive cardiac stimulation producing either an abnormally quick diastolic relaxation and a consecutive sudden passive tension of the ventricular wall from the entering blood, or an increased contraction of the auricle.

(B) Blood Vessels

1. The subjective symptoms referable to the blood vessels are numerous and interesting.

(*a*) Those of the neck are chiefly (i) throbbing sensations of the thyroid gland itself because of the great increase of vascularity in the organ. The arteries, veins, and lymphatics are not only more numerous but markedly dilated so that occasionally the patient experiences a throb of the gland with each cardiac systole. (ii) If the thyroid is very large, the patient will also experience pressure symptoms of the trachea, esophagus, and in some instances of the carotid sheath, resulting in dysphagia, dyspnea, altered voice, vertigo, headache, and even moments of syncope. Rarely epistaxis occurs from congestion of the nasal mucosa.

(*b*) The throbbing sensations in the other large vessels of the body (carotids, subclavian, radial, ulnar, femoral) are often so marked as to simulate the throbbing which commonly occurs in aortic regnrgitation. This symptom occasionally gives rise to complaints almost as marked as the palpitation.

2. Of the objective symptoms pertaining to the blood vessels, those of (*a*) the neck require careful observation. *Inspection* reveals a large thyroid in most instances. In the presence of markedly increased vascularity, the greatly increased superficial veins will be seen coursing beneath the skin. On close observation the thyroid itself will be observed to throb with each cardiac cycle. As in the case of aortic regurgitation, the large blood vessels of the body are seen to throb with the heart and often the jugulars also. *Palpation* of the thyroid usually presents a systolic thrill. The thyroid pulsations, as felt by the palpating hand, are almost as expansile in character as those of an aneurysm. A moderate amount of pressure may elicit tenderness. The grasping of the entire thyroid by the observer frequently causes a partial diminution in size of the gland because of expression from it of a quantity of blood; in this respect a Basedowian thyroid gland may be compared to a sponge. Occasionally, a venous pulse of the jugular veins may be felt, usually diastolic in time. *Auscultation* over the thyroid reveals a harsh murmur, usually systolic, occasionally also diastolic. This is almost path-

ognomonic of a hyperacting thyroid gland and is a point to be remembered in differentiating the mass from a simple or nontoxic goiter. The large vessels of the neck, especially the carotids and the subclavians, also give rise to a systolic and occasionally diastolic hum. "The systolic murmurs are arterial, depending upon the *pulsus celer*. It is not decided whether the diastolic are arterial resulting from the *pulsus celer* or whether it is a diastolic portion of venous murmurs isolated and strengthened because the veins are compressed or closed by the arteries during systole"—(Sahli).

(*b*) The objective symptoms of the arteries elsewhere include in addition to (i) the throbbing of the superficial arteries. (ii) The capillary pulse which resembles that found in aortic regurgitation and may be elicited over the finger tips or by pressure of a glass slide upon the inner side of the mucous membrane of the lips. (iii) The pulse of these patients is usually small, rapid, and of poor volume, varying with the stage of the disease and the degree of repose of the patient. It is often dicrotic, and in advanced cases with cardiac embarrassment arrhythmia may occur. (iv) Dermographia is usually present and is very typical. The vasomotor instability is further emphasized by the frequent occurrence of large erythematous areas of the skin. (v) The blood pressure is at first somewhat higher than normal because of the more vigorous action of the myocardium. With the weakening of the heart through dilatation and the occurrence of circulatory relaxation, the pressure is lowered, reaching 130 to 120 mm., and as this process continues to cardiac insufficiency, the systolic pressure may come down to 100 or even 90 mm. associated with considerable cyanosis and dyspnea.

(C) The Blood

1. Generally speaking, the subjective symptoms referable to the blood in exophthalmic goiter are those of a degree of secondary anemia. The intoxication, the poor re-

spiratory expansion, the depraved nutritional status, all conspire toward a blood impoverishment which on inspection may not be evident. There is no doubt that the weakness of which the patient complains is, in part at least, due to this secondary or symptomatic anemia, though as a rule, the latter exists only in a moderate or mild degree and does not form an essential feature of the subjective phenomena.

2. The objective points with regard to the blood are inconstant. Leucopenia is a more or less pathognomonic feature in diseases of the thyroid gland and is quite constant in Graves' disease. The white blood cells may be reduced to 6,000 or even 5,000 per cubic mm. A relative lymphocytosis occurs concomitantly with the leucopenia; the increase may be up to 50 per cent, the small lymphocytes predominating. There is a diminution of the polymorphoneutrophiles.

According to Kocher, the findings upon examination of the white blood cells are caused by the presence of an increased quantity of thyroid secretion in the blood stream, resulting in a stimulation of the lymphatic system. A similar blood picture results from the intravenous injection of thyroid extract. It seems reasonable to assume that the lymphocytosis may be due to another of the vicious circles so often mentioned in descriptions of Graves' disease and possibly directly due to the hyperactivity of the enlarged thymus gland. The increase in size of the thymus may be caused by the thyroid hyperfunction, the excess of thyroid substance in turn stimulating the growth of the thymus.

Crotti claims that the intensification of the white blood corpuscle picture of Graves' disease is an indication of a poor prognosis; a high lymphocyte percentage with a moderate leucopenia is a good prognostic indication; the reverse is claimed in the presence of marked leucopenia and a low lymphocyte percentage. The persistence of an abnormal blood formula, as above indicated, is said to prove a remaining degree of thyroid intoxication or possibly a gradual passing of the hyperthyroidism into hypothyroidism. Marine and Lenhart state that there is a close parallelism between the percentage of mononuclear cells in the circulating blood and the extent of the active lymphoid and thyroid hyperplasia, so that the blood examination is a fairly accurate clinical means of judging the extent of active lymphoid and thyroid hyperplasia and a fair index of the severity of the disease, though in no sense specific of exophthalmic goiter.

The red blood corpuscles are practically normal in early cases of hyperthyroidism. In fairly advanced cases the number may be reduced to four million or less, with a greater diminution of hemoglobin, resembling the picture seen in chloroanemia. The increased oxidation occurring in the metabolic processes of the patient's tissues and the vasomotor instability may give rise to a false appearance of plethora, since many of these patients possess rosy cheeks, masking the true state of affairs.

Hemorrhages from the nose, stomach, lungs, and bowels, often to a dangerous degree, may occur in isolated instances, and are probably due to local vasomotor paralysis and diminished viscosity of the blood. Diminished coagulability is a quite constant finding in hyperthyroidism and explains the difficulty of controlling hemorrhage in many instances of thyroidectomy. The determination of the degree of coagulability of the patient's blood is not only a diagnostic factor, but occasionally of prognostic value from the viewpoint of operative recovery of the patient.

Hyperglycemia is an important observation, as the Basedow patients are to a degree intolerant to carbohydrates. Ordinarily, the ingestion of 100 gm. of sugar causes no increase in the normal individual's blood, the sugar content of which is about .085 per cent. In a Basedow subject, the ingestion of this quantity of sugar increases the normal content to about double. The ingestion of large quantities of the extract of the thyroid gland yields the same result.

The hyperglycemia can not be said to be of primary, but of secondary or alimentary origin.

Lampa and Deutsch (quoted by McCarrison) have obtained, by means of Abderhalden's reaction, results which appear to indicate the presence in the serum of sufferers from Graves' disease of special ferments which act on the ovaries, the thyroid and the thymus, but on no other organs. Kraus states that the serum causes dilatation of the pupil of the enucleated frog's eye.

Sanford and Blackford have described a potent depressor substance existing in the blood of sufferers of Graves' disease, acting in many respects similar to peptone in 10 per cent solution. McCarrison suggests that this substance is derived from the gastrointestinal tract.

The Thyroid Gland in Exophthalmic Goiter

For clinical purposes and with a view to simplifying the diagnosis of primary, toxic goiter, I would suggest the following classification of affections of the thyroid:

(*A*) Primary, hyperplastic goiter (exophthalmic goiter, Graves' disease, Basedow's disease, etc.)

(*B*) Nonhyperplastic goiter (capable of becoming "Basedowified")
  1. Simple, "nontoxic" goiter
  2. Thyroiditis
  3. Carcinoma (and sarcoma)
  4. Syphilis
  5. Tuberculosis

(*C*) Intrathoracic goiter. This may be of the (*A*) or (*B*) type.

(*D*) Affections of the accessory thyroids. These may also be of the (*A*) or (*B*) type.

(A) Primary, Hyperplastic Goiter

(Exophthalmic Goiter, Basedow's Disease, Etc.)

It is well-known that the thyroid gland need not be visibly nor palpably enlarged to be in a state of hyperfunction. A large number of cases of Graves' disease possess no gross evidences of increased size in the gland. This does not mean, however, that the thyroid is not enlarged. Kocher's dictum, "no goiter, no Graves' disease," is not an assumption that if visibly and palpably there is no increase in the size of the thyroid, the same does not exist and consequently there is no Graves' disease. The thyroid gland may increase in size by growing "inwardly" or substernally, or in rare instances, there may be hypertrophy of an accessory thyroid situated somewhere in the neighborhood of the tongue, larynx, trachea, or mediastinal regions. Occasionally, in these instances the patient may complain of choking sensations because of pressure, and rarely of a dry, hacking cough. Sometimes, the thyroid hypertrophy will be so insidious and inapparent as to be detectable on microscopic examination only. It must not be forgotten that especially at first, a thyroid may hyperfunctionate without any apparent increase in size, constituting the early or incipient case of Graves' disease, the time when diagnosis is most important and most productive of therapeutic results.

The question of whether some of these instances of Graves' disease unassociated with any visible and palpable enlargement of the thyroid are really due largely to a disturbance of the other glands of the body, such as the thymus, pituitary, or ovarian glands, is one which can not yet be answered, and for a discussion of which the reader is referred to the chapters on physiology and etiology.

The facts in the matter may be summed up as follows:

1. The thyroid may be physiologically enlarged without evidences of hyperaction, *e.g.*, during menstruation, pregnancy, mental and physical excitation, adolescence, menopause, the various infections, etc., which enlargement usually disappears on the disappearance of the cause. These variations in size and even function without appreciable symptoms are so common that it is often impossible to sharply differentiate between a normal and an abnormal thyroid.

2. The thyroid may be apparently normal (10 to 30 per cent, varying with the experience of different observers)

and be hyperactive, proving that goiter is not essential to the existence of a well-marked Basedowian syndrome.

3. The thyroid may be slightly enlarged during moments of physical or mental excitation and during the existence of other causes of thyroid engorgement, to resume its former size on the disappearance of said causes, in the presence of an incipient form of Basedow's disease. The heart rate may mount to 90 or 100 day and night, there may be a hyperexcitability of the bodily activities, especially of the nervous system, and a gradual decline in weight and vitality; this, in brief, is the *fruste* form.

4. In the majority of cases, the thyroid gland is quite perceptibly enlarged, but not excessively so, at the same time presenting unmistakable evidences of exophthalmos, mental alertness, emaciation, and on close examination, the various other signs and symptoms of exophthalmic goiter.

5. The thyroid gland may never increase in size, perceptibly or imperceptibly, and yet, all the other evidences of Basedow's disease may exist; these are instances in which, very likely, one or more of the so-called accessory thyroids anomalously placed by nature have undergone hyperplasia.

It can be concluded, then, that the absence of goiter does not mean the absence of hyperthyroidism in the clinical sense, and shows off in bold relief how fallacious it is to employ the term of exophthalmic goiter for the Basedowian syndrome. In approximately 80 per cent of cases, however, thyroid enlargement, varying from a slight fullness to an appreciable goiter will precede, accompany, or follow exophthalmos and tachycardia.

In the average case of exophthalmic goiter, some time after a period of palpitation and general nervousness, the patient begins to observe that the neck becomes rather full in front: a male will find his collars too small; a female that high-necked dresses do not fit. Soon it is found that manipulations about the front of the neck (washing, clothing, and so on) elicit a feeling of uneasiness, occasionally tenderness. In course of time it may be discovered that the voice changes, a degree of hoarseness ensues, frequent clearing of the throat is necessary, sometimes cough and expectoration occur, and the voice easily tires. Occasionally some dysphagia, especially on swallowing a large bolus, and rarely dyspnea occurs if the goiter is large or if it is intrathoracic.

On physical examination of the goiter, the following signs are usually elicited:

Inspection.—The size is usually small, from almost normal to marked goiter, never assuming the large proportions of simple or nontoxic goiter, unless undergoing secondary changes.

The shape usually conforms diffusedly to the horse-shoe area of the thyroid gland. Occasionally, the isthmus is more prominent than the horns; more frequently the right lobe presents greater hypertrophy than the left. The right lobe, if hypertrophied, remains so a greater time than the enlargement of the rest of the organ and occasionally for some time after the amelioration of all symptoms.

Mobility.—It moves up and down with movements of the larynx, and of course, with deglutition. The skin moves freely over the goiter. A "suspicious" or very slight enlargement is made very much more prominent by having the patient hyperextend the neck and swallow, when the enlarged thyroid will be seen and felt by the examiner to follow movements of deglutition.

Throbbing may be seen in highly vascular goiters, corresponding to cardiac cycles. This may be associated with throbbing of the entire body. The vessels are markedly dilated and seen coursing beneath the skin. These may throb on inspection, which may appear as a part of the general vascular throbbing (subclavians, carotid, jugulars, etc.).

Palpation confirms inspection regarding size, shape, symmetry, mobility, vessels, etc. The mass is usually soft and yielding, but occasionally undue resistance is offered to the palpating fingers because of fibroid changes occurring within the gland (especially in the aged). In these instances the possibility of malignant changes must be borne in mind.

Tenderness is usually elicited on deep palpation.

Throbbing and thrill are quite characteristic.

Compressibility and Elasticity.—Grasping the thyroid, the examiner may, by moderate compression, expel a quantity of the blood in much the same manner as one expresses water from a distended sponge.

Auscultation.—There is a bruit, systolic, rather sharp and loud, simulating that observed over an aneurysm. Some observers claim to have heard the thyroid bruit at a distance from the gland. Due to the marked arterial vascularity, the gland acts in a manner similar to that of a second heart in advanced cases. The diastolic bruit is not quite as loud as the systolic and not as constant, and is due to tricuspid regurgitation. The combined systolic and diastolic murmur is somewhat similar to that heard over a double mitral or tricuspid murmur, excepting that the sounds are harsher and less musical in quality.

(B) Nonhyperplastic Goiter

1. Simple or Nontoxic Goiter.—In brief, the differential diagnosis between a simple or nontoxic and a hyperplastic or toxic goiter could be summed up in one sentence: In the subject of simple goiter there is *nothing* wrong but an enlarged thyroid; in the subject of exophthalmic goiter, *everything* is wrong. To be more specific, the following tabulation will assist us:

Simple or Nontoxic Goiter	*Exophthalmic Goiter*
(*a*) Frequently a history of goitrous geographical location or numerous pregnancies, not dependent upon shock or neurotic tendencies.	History of nervous shock, fright, or a neurotic tendency.
(*b*) Tendency to distinct circumscription frequently beginning as an egg-shaped tumor over the isthmus, often assuming markedly noticeable proportions.	Enlargement is diffuse, smooth, round, often a mere thyroid fullness, rarely assuming a size perceptible at a distance.

Simple or Nontoxic Goiter	*Exophthalmic Goiter*
(*c*) Comparatively rapid growth.	Comparatively slow growth.
(*d*) Pressure symptoms common.	Pressure symptoms rare.
(*e*) Barely compressible and tender on palpation.	Usually compressible and tender on palpation.
(*f*) Pulsation, thrill and bruit rare.	Pulsation, thrill and bruit characteristic.
(*g*) Usually no weakness or emaciation.	Marked weakness and emaciation.
(*h*) No cardiovascular, nervous, ocular, gastrointestinal, cutaneous or urinary manifestations.	Characteristic cardiovascular, nervous, ocular, gastrointestinal, cutaneous and urinary changes.
(*i*) No change in thymus.	Thymus enlargement often occurs.
(*j*) Often improved by administration of thyroid extract or the iodides.	Symptoms markedly aggravated by thyroid extract and often by the iodides.

1. "Secondary Basedow" or "Basedowified" Goiter.—In the presence of goiter, inroads are often made by the neoplastic tissue upon the thyroid tissue. This encroachment may or may not stop short of allowing a sufficient amount of thyroid tissue for the normal body requirements. But who can tell where the process stops? Often we find symptoms of myxedema gradually supervening in a patient who has had an "innocent" goiter for years. Such a case presents a difficult problem for solution. The questions of whether to operate and how, whether and how to administer thyroid extract, the iodides or both, and many other perplexities now present themselves.

Occasionally, the "innocent" goiter, having existed for years without harm, will, through shock, physical or mental overexertion, pregnancy, infection, or some unknown cause, instigate a *hyperplastic* change in the healthy portion of the thyroid gland with a resulting mild or severe syndrome of Graves' disease. These are the so-called "secondary" or "Basedowified" forms of the disease, described by Pierre Marie. Here again we face a serious problem. Should we combine the iodine therapy with the treatment empirically calculated to antagonize the hyperthyroidism? Will not the iodine treatment interfere with the efforts antagonistic to the hyperthyroidism? Or, should we first operate, removing the original goiter as far as could be calculated, then institute the necessary nonsurgical treatment of hyperthyroidism?

Not rarely do we find ourselves confronted with the most complex of all these problems, the incidence of a combination of hyper- and hypothyroidism during the course of a simple goiter. Here the question is the most complicated of all and one which we merely mention in passing.

Hyperfunction may occur in any thyroid gland, goiter or no goiter, but the presence of a previous growth, even though inactive for years, may instigate a hyperplastic process with consequent symptoms of hyperthyroidism on the one hand, or a hypoplastic process with resulting hypothyroidism, on the other. The thyroid in simple or nontoxic goiter may under excitement or other unknown causes begin to pulsate, presenting vaguely some suggestions of Graves' disease, which may disappear with proper rest and equanimity of body and mind, the case soon assuming the picture of simple goiter. These are the "borderline" cases, and the frequent recurrence of the syndrome, be it ever so mild, may soon terminate in permanent, secondary Graves' disease.

The differentiation between a primary and secondary Basedow syndrome is not difficult.

Secondary Basedow	*Primary Basedow*
(*a*) History of preexisting goiter for years past.	No such history.
(*b*) Goiter large and resisting.	Goiter, if present, is of recent occurrence, soft and compressible.
(*c*) Pressure symptoms frequent.	Pressure symptoms rare.
(*d*) Exophthalmos, if present, not marked.	Exophthalmos usually present and quite evident.
(*e*) Evidences of "toxic heart" for some months or years past.	Not so. Recent occurrence of palpation, tachycardia, etc.
(*f*) Nervousness and emaciation not marked nor rapidly progressive.	Nervousness and emaciation are prominent symptoms and rapidly progressive.

There is still another way in which a simple goiter may bring about a syndrome resembling Basedow's disease. We have observed that by an internal change the nontoxic goiter becomes toxic or Basedowified. A large simple goiter or a small one by virtue of its location, *without* undergoing hyperplastic changes may, by pressure upon the cervical sympathetic, give rise to palpitation, tachycardia, and exophthalmos. These symptoms need not depend for their causation upon a thyroid enlargement, but may also be produced by any mass or tumor in the neck or mediastinum. The symptoms in this form of "false Basedow" are easily distinguished from those of hyperthyroidism: in the former, there is usually a unilateral exophthalmos, unequal pupils, pallor of cheek of the affected side, and little or no excitation of the nervous system. During the stage of paralysis of the ganglia, there is ptosis of the affected eyelid with a smaller palpebral fissure, myosis, redness of the ear and perspiration on the affected side of the face.

It might here be remarked that the surgical cures of exophthalmic goiter,—cures which *could* be demonstrated, are accomplished in cases of "false Basedow" or "Basedowified goiter." The removal of the pressure upon the cervical sympathetic, on the one hand, or the removal of the trouble-producing heretofore "innocent" goiter, on the other, eliminates the cause of the syndrome, and we have a brilliant cure. But a given case of this sort is obviously not a case cured of genuine primary exophthalmic goiter or Graves' disease, but merely a successful removal of a simple, long-standing goiter.

2. Thyroiditis.—An acute infection of the thyroid, usually secondary to a local infection elsewhere or to an acute infectious disease, is also capable of giving rise to secondary Basedowian symptoms. An attack of thyroiditis is usually heralded by chilliness, high fever, pain in the region of the thyroid spreading to the shoulders and the nape of the neck and accompanied by swelling and diffuse puffiness of the thyroid area. Dysphagia and dyspnea are variable in degree and at times alarming. If to this picture is added persistent tachycardia, tremor, nervous excitation, not receding on the disappearance of the thyroid inflammation, we are soon face to face with a typical case of Graves' disease. This may occur during the course of or immediately following a thyroiditis of traumatic origin, or such local infections as tonsillitis and mastoiditis, or as a complication or sequel to acute articular rheumatism, typhoid fever, influenza and the like.

3. Carcinoma of the Thyroid.—The diagnosis of an early case of malignancy of the thyroid—the period when surgery is most productive of good—is extremely difficult. When the diagnosis is quite evident, we are dealing with an advanced and practically inoperable case.

Balfour suggests that the frequency of cancer of the thyroid as compared with benign enlargements of the gland can only be estimated, since an unknown and probably a relatively small percentage of the so-called simple goiters of patients seek medical or surgical advice. He states that of 6, 359 cases of goiter, exclusive of the exophthalmic group, seen in the Mayo clinic during the six years from January, 1910, to January, 1916, 103 cases were classified as cancer. The cancer incidence based on all patients with goiters (14,456) coming to the clinic from January 1, 1910, to August 1, 1918, is 1.19 per cent. The age incidence in the 103 cases is:

8 cases (7.9 per cent) between 20 and 30.
10 cases (9.6 per cent) between 30 and 40.
30 cases (29.1 per cent) between 40 and 50.
30 cases (29.1 per cent) between 50 and 60.
25 cases (23.3 per cent) more than 60.

Eighty-one and one-half per cent of the 103 patients were more than forty years of age. Sixty-eight (65 per cent) were females, thirty-five (35 per cent) were males. In almost every case there was a history of a long preexisting goiter. As pointed out by Plummer, the disease has never, in the experience of the Mayo clinic, developed in a distinctively and purely hyperplastic gland. This is a very important observation, since many subjects of exophthalmic goiter are urged to an unnecessary operation because of the fear of future cancerous changes within the gland.

Crotti states that in a large majority of cases, malignant disease of the thyroid gland is superimposed upon a previously existing goiter occurring usually at about the age of fifty, though rarely sarcomatous goiters are found in children. In the goitrous districts, malignant goiter is more frequently found in women than in men and occurs mostly at the menopause, hence the absolute necessity of removing any goiter which begins to grow at that time of life.

Though incipient malignancy of the thyroid is detected with difficulty, it is not difficult to distinguish between a primary hyperplastic thyroid and one undergoing carcinomatous changes. Usually the following is the course of events: A goiter of long standing which has been stationary in size for years, suddenly begins to grow more rapidly. Soon, usually within a few weeks, the growth becomes more resistant to palpation and adherent to the overlying skin; it is tender to the touch, and shooting pains are felt along the cervical regions upward toward the ears and downward toward the shoulders and arms. These phenomena are quite significant and should at once arouse our suspicions. The mass becomes progressively harder, the skin more swollen and infiltrated; pressure on the esophagus and trachea soon supervenes, giving rise to dysphagia, hoarseness, and distressing cough. During all this time the patient develops the characteristic facies of malignancy: there is marked cachexia, anemia, insomnia and restlessness. Sooner or later the patient suffers from paroxysms of choking; the pressure upon the larynx, trachea, and inferior laryngeal nerves becomes extreme, leading occasionally to nearly complete obstruction or perforation; rarely perforation into a great vessel causes fatal hemorrhage. The usual patient dies of dyspnea, starvation, or during a paroxysm of choking.

Though carcinomatous changes rarely, if ever, occur in a strictly hyperplastic or Basedowian thyroid, there is occasionally seen a *Basedowified cancer,* that is, the occurrence of hyperplastic changes and the syndrome of hyperthyroidism during the course of thyroid malignancy. In the presence of the combination of malignant disease and the Basedowian syndrome sometimes one phase, and sometimes the other may become more prominent. Occasionally, if the symptoms of exophthalmic goiter attain the ascendency, it is difficult to detect the presence of malignancy unless a portion of the tumor is examined microscopically.

4. Syphilis of the Thyroid.—Simonton asserts that syphilis as a factor in diseases of the thyroid gland does not command the attention it deserves. The finding of a positive Wassermann reaction and the application of the therapeutic test are conclusive, and Simonton believes that if these were done routinely the condition would be detected more often than it is today. This author reports several cases of toxic and nontoxic goiter cured by means of the combined salvarsan and mercurial treatment. Abrahams, von Pezhold, Sainton and Bernhardt also report cases of successful cure of toxic goiter by specific treatment. It is not improbable that some of the cases of exophthalmic goiter which responded so promptly to iodine therapy in my experience and in the experience of others, were of syphilitic etiology.

5. Tuberculosis of the Thyroid.—The relation of tuberculosis to Basedow's disease has been the subject of comment by many observers. Tuberculosis of the lungs and elsewhere is seen to occur in subjects of Graves' disease with relative frequency, in many clinics. Cases of associated pulmonary tuberculosis have been described by Knopf, Bialokur, Swan and others. Cases of definite tuberculosis of the thyroid gland are, however, rarely met with. In other words, many patients are seen who are tuberculous and are suffering with Basedow's disease at the same time, but very few have presented the specific tubercles within the thyroid substance. Eminently among the cases reported in literature is one of Gilbert and Castaigne, quoted by Roussy, in which the tubercle bacilli were found in the thyroid gland.

(C) Intrathoracic Goiter

A goiter lying below the suprasternal notch, *i.e.*, within the thorax, is termed an intrathoracic goiter. A goiter may be only slightly intrathoracic, extending downward from the thyroid area to just within the mediastinal space. Or, it may be almost totally intrathoracic and engender dangerous pressure symptoms. Between the two extremes, we find varying degrees of "dipping" of thyroid neoplasms into the thorax.

Intrathoracic goiters are almost never primarily hyperplastic. They are benign growths which are harmless for a while until they assume size enough to cause pressure symptoms, when the evidences of mechanical "goiter heart" become prominent. Frequently the pressure upon the trachea, esophagus, nerve structures and great vessels is so great as to render the immediate removal of the growth a vital necessity.

As in the case of ordinary simple goiter, an intrathoracic goiter may instigate hyperplastic changes in the thyroid and give rise to secondary Basedowian symptoms. Occasionally, a "Basedowified" intrathoracic goiter may also give evidences of mechanical toxic heart,—a very interesting and complicated combination. Rarely, especially in older patients, malignant changes will supervene.

The diagnosis of intrathoracic goiter is accomplished by a consideration of the history, a careful physical examination, and an x-ray observation.

(D) Accessory Thyroid Goiter

Accessory thyroid goiters occur in thyroid tissue anomalously placed,—at the root of the tongue, about the trachea, in relation with the aorta, and elsewhere in the mediastinal spaces. These may undergo the changes incident to simple goiter and become "Basedowified," or become primarily hyperplastic with evidences of hyperthyroidism, or rarely may become primarily or secondarily affected with malignancy.

Accessory thyroid growths are extremely rare, and when they do occur are difficult to diagnose,—even x-ray examination often does not assist us materially. In a patient suffering from unmistakable evidences of Graves' disease in whom the thyroid seems *entirely* normal even late in the disease, the possibility of an existing hyperplastic accessory thyroid must be borne in mind.

The Eyes in Exophthalmic Goiter

Next in importance to the study of the thyroid gland, the eye symptoms deserve our attention in the study of Graves' disease.

Exophthalmos.—It is the bulging forward of the eyeballs characterizing both fright and hyperthyroidism, that gave rise to the term exophthalmic goiter, and led a large percentage of observers, both orthodox and modern, to attribute the disease to shock to the emotions.

In 1882, Claude Bénard confirmed the observations made in 1873—namely, that irritation of the sympathetic produced exophthalmos, and that section of the ganglion overcame the ocular protrusion. In accordance with Trousseau's theory that exophthalmic goiter is due to a disturbance of the cervical sympathetic, Jaboulay, and later Jonnesco and others, operated on the sympathetic with a view to curing the syndrome. Although the exophthalmos was reduced to a marked degree in many cases, the operation is now practically discarded as impracticable.

It was formerly thought that exophthalmos was a *necessary* sign of Graves' disease, and in its absence, the syndrome was to be looked upon as an evidence of another affection. We now know that in from 10 to 30 per cent of cases of the disease exophthalmos is absent.

Exophthalmos occurs sooner or later in from 70 to 90 per cent of cases. It may occur early and suddenly in instances where extreme fright or terror is responsible for the syndrome, as, for example, the explosion of a bomb or the participation in a runaway. In the usual case, however, this symptom is gradual in coming, occurring months after the onset of the cardiac and nervous phenomena.

At first, there may be merely an unusual stare of the eyes during active attention and conversation, and this, plus the moodiness and nervousness, causes the family to suspect that the patient is becoming "queer." This stare soon becomes permanent and more marked than ever, until in course of time the relatives and friends of the patient are more or less alarmed about his expression. This bulging of the eyeballs may at times become so marked as to render the closing of the eyes impossible, so that the patient is obliged to sleep with the eyes partly open.

The degree of exophthalmos varies with the severity and the duration of the disease, and though it may not fluctuate to the extent of the vacillations seen in the enlarged thyroid, yet it is seen to vary temporarily and become exaggerated during excitement, exertion, active attention and menstruation. These factors may increase the protrusion of the eyes until they seem ready to "pop out." Indeed, in rare cases there is no discernible cause for a rather malignant progress of exophthalmos in which, though the progress of other evidences of the disease has apparently been checked, the eyes continue to bulge more and more forward, leading to very sad consequences. I have seen a case in which, after the use of thyroid extract as a therapeutic (!) measure, a double enucleation became necessary to save the life of the patient because of a virulent infection of the eyeball resulting from ulceration through congestion (passive) and exposure. In a recent case of mine which completely recovered, the patient was obliged to place small pads of lint over her eyes at bedtime for protection from exposure. Through patient, untiring efforts, by means of hygienic, dietetic, medicinal, and electrotherapeutic measures, the amelioration of her condition brought about a complete cure of the syndrome within six months.

Occasionally the exophthalmos is more marked on one side than on the other, or it may occur on one side only, and in rare instances, it may be unilateral for a long time and finally, the other eye will become affected to an equal or unequal degree.

The exophthalmos (like the goiter) is among the last of the symptoms to disappear during the improvement of the patient, and it may take months or even a year or two after the disappearance of the other symptoms for the eyes to resume their normal appearance. Occasionally one eye may improve more rapidly than the other.

The *modus operandi* of the exophthalmos is still a matter of controversy and interesting speculation. It is thought that this phenomenon is due to one or more of the following factors:

A deposit of fat behind the eyeball.

Continuous contraction of the levator palpebrae muscle causing a contraction of the lids and exposure of the sclera.

Venous congestion of the posterior part of the orbit. J. C. O'Day believes that the exophthalmos is due to stasis in the ophthalmic veins, due in turn to "tetany of the ventricles."

Dilation of the retrobulbar arteries.

Contraction of Muller's muscle. This latter consists of a small group of muscular fibers located between the sphenomaxillary fissure and the supraorbital groove.

Landstrom (quoted by C. H. Mayo) describes a microscopic muscle occurring in streaked layers in the fascia behind the eyeball and about the globe. This muscular sheath is attached forward to the lids and anterior orbital fascia. It is controlled by the sympathetic nervous system and serves to oppose the four orbital muscles which draw the eyeball back. Irritation of Landstrom's muscle directly or through the cervical sympathetic causes exophthalmos and the concomitant drawing backward of the lids. This phenomenon is produced with the assistance of Muller's muscle.

Maurice believes that the exophthalmos is probably due to an excessive action of the adrenals.

Marine and Lenhart, however, conclude that in view of the fact that exophthalmos may occur without thyroid hyperplasia and that there may be a marked thyroid hyperplasia without exophthalmos, "both phenomena, though often not synchronous, are manifestations of a fundamental and more obscure nutritional disturbance." These authors believe that the thyroid hyperplasia is not a direct etiologic cause of exophthalmos.

Exophthalmos from Other Causes.—Exophthalmos is most common in Graves' disease. A few other conditions may at times simulate the exophthalmos of exophthalmic goiter:

Extreme fright, in which the physiognomy assumes a picture of terror and the body is in an attitude of self-defense. Here the condition is bilateral and disappears on the passing away of the cause of the emotional strain.

Where the exophthalmos is so slight as to render its existence questionable, it is important and often difficult to differentiate it from the ocular protrusion of marked myopia.

Exophthalmos resulting from an irritation or pressure of the cervical sympathetic is usually unilateral, occurring on the same side as the irritated ganglion. This, among other causes, may be due to pressure from a nontoxic goiter, in which case the condition may be bilateral and with great difficulty differentiated from the exophthalmos of hyperthyroidism.

Attacks of bronchial asthma and angina pectoris, during the seizures, are often accompanied by a degree of exophthalmos, depending on the degree of dyspnea present.

The same may be said of other causes of dyspnea, *e.g.*, organic heart disease, and marked acute pulmonary embarrassment.

Thrombosis of the superior longitudinal sinus may give rise to a slight exophthalmos, unilateral or bilateral. There may be an apparent bulging of the eyes in paralysis of the ocular muscles.

An acute recurrent exophthalmos due to angioneurotic edema has been described. (Gruss.)

A pathologic state within or behind the orbital cavity, such as marked enlargement of the lachrymal glands, tumor or aneurysm within the orbit or of the upper jaw bone, within or outside of the antrum of Highmore, and hydrocephalus may give rise to this bulging of the eyeball. Chloromatous masses are especially liable to the causation of ocular protrusion. (Dock).

Pulsating exophthalmos may be due to aneurysm of the ophthalmic artery inside or outside of the skull, pulsating orbital tumors, aneurysmal dilatation of the internal carotid artery in the cavernous sinus, thrombosis of the cavernous sinus and ophthalmic vein, arteriovenous aneurysm of the orbit, pressure on the sinus by an external growth, and rupture of the internal carotid into the cavernous sinus.

I have seen a case of cyst formation in relation with the frontal bone causing pressure upon one orbit with resulting protrusion forward of the corresponding eyeball.

We must also bear in mind that a slow or a sudden hemorrhage within the orbital cavity or any other substance, liquid or solid, accumulating within the orbit would tend to displace the eyeball forward.

It is not necessary to dwell in detail regarding the differential features distinguishing the exophthalmos of hyperthyroidism from the bulging eyeballs of other conditions. In hyperthyroidism the condition is usually bilateral and insidious in onset; it is usually not attended with any pain, is usually preceded and almost always accompanied by one or more of the recognized cardinal symptoms; there are the various classical signs (Von Graefe's, Stellwag's, Moebius', Dalrymple's, etc.,) and there is the absence of other causes of exophthalmos.

Stellwag's Sign (staring eye).—This sign consists of imperfect power of winking or diminished frequency of the act. There may be a number of rapid winks succeeded by a long pause in which there is no movement of the lids. Each wink is incomplete; the margins of the lids do not come together as in the normal eye. This absence of normal involuntary winking may be an early sign, the patient not winking for minutes at a time, and then incompletely.

Dalrymple's Sign.—This consists of retraction of the upper lid so that there is an undue separation between the two lids. The resulting widening of the palpebral fissure produces the peculiar stare which is present in Graves' disease, somewhat similar to the effect produced by cocaine.

Von Graefe's Sign.—In the early recognition of the disease this sign is important. In a normal eye, when the globe is directed downward the upper lid moves in perfect accord with it. In subjects of Graves' disease, the upper lid follows tardily the downward movement of the eyeball, or having begun its downward course stops short of completion, the eyeball alone continuing downward, or, in some cases the upper lid does not move at all. This symptom is not constant, but is almost always a precursor of exophthalmos, and persists after the subsidence of protrusion of the eyeballs.

Solomon Solis-Cohen describes what he terms the "hitch" sign of the upper eyelid which he considers the "larval" form of Von Graefe's sign. When the eyelid begins its downward course over the eyeball it stops short (the "hitch"), then proceeds downward to imperfectly conclude its descent. When the lid is again raised, it does so not with a continuous movement, but presents a sudden hesitancy or "hitch" in its upward course.

Moebius' Sign.—Moebius' sign consists in a diminution or absence of convergence. To test the convergence near point, approach a finger or pencil to the nearest point upon which the eyes can converge, which normally should be situated at no greater distance than 3 1-2 inches from the eyes or about 1 1-2 inches from the nose. If outward deviation of an eye occurs before this point is reached, convergence is deficient. Paresis of the ocular muscles is more characteristic than mere insufficiency of convergence (Heerfordt).

Kocher's Sign.—Kocher's sign is a slight momentary retraction of the upper eyelids on gazing at some object, if the latter is moved up and down. The upper lid rises abruptly upward, ahead of the upward movement of the eyeball, when following the object.

Tremor.—Tremor of the eyeballs is an occasional marked sign.

An almost constant sign is the presence of a rim of white above and below the cornea.

Ulceration.—Ulceration of the cornea, as intimated, is not an uncommon occurrence. The function of the eyelids as protectors of the delicate ocular conjunctiva being diminished, the lids being unable to close over the protruding organ, the eyeball is exposed to the air day and night; indeed, even winking is for that reason less frequent and less complete. As a result of this exposure, chronic conjunctivitis and corneal ulceration may occur, leading frequently to partial or complete blindness, and, if infection becomes marked, to panophthalmitis, so that an urgent necessity for enucleation may arise.

Suker (quoted by Zentmayer) has recently described another ocular symptom of hyperthyroidism. After extreme lateral rotation of the eyes to the right or to the left with the head fixed and with fixation of an object at this point maintained for a second or two, on attempting to follow this fixation point as it is rapidly swung into the median line, one or the other of the eyes *fails to follow its fellow* in a complementary manner into proper convergence and for this point, when it is brought into the median line. Either the right or the left eye makes a sudden rotation into the fixation with its fellow, but before it does so, an apparent divergent strabismus is manifested. Suker believes this phenomenon due to a dissociation in the functions of the sympathetic and the extraocular motor nerves of the eye, and perhaps also to exhaustion on extreme lateral rotation of the eyes.

The Jellinck-Teillais Sign.—This sign is a brownish discoloration of the eyelids and is seen as a ring around the orbit. The discoloration is of a deep brown, occasionally almost violet hue and occurs in 10 to 25 per cent of all cases of hyperthyroidism. Sainton and Fayolle state that it is often a feature of the earliest stage of the disease, later almost disappearing, with subsequent recurrence. Brown spots elsewhere on the body may coexist, suggesting the stain of iodine on the skin.

A not uncommon phenomenon is a *falling out of the eyebrows* and eyelashes, which is an accompaniment of the alopecia frequently met with in hyperthyroidism.

Nystagmus.—This is rarely observed.

Difficulty of Everting the Upper Lids.—This phenomenon is an almost constant sign (Goffre).

A subjective feeling of *pressure* behind the eyes is described by A. Kocher.

Preble notes an abnormal *dryness* of the eyes in a certain percentage of cases.

On the other hand, *epiphora* or abnormal *lachrymation* is seen in many instances.

Reisman describes a *bruit* over the eyeball, synchronous with the heart beat. The bowl of the stethoscope is placed over the closed eyelid. The phenomenon is inconstant. The same sign is obtainable in aortic regurgitation. Reisman does not claim priority in the detailing of this sign, stating that it has been reported by Snellen, Donders, Hunter, Carrington and Drummond. E. Herring claims that murmurs over the eyeball are of muscular origin, heard when the eyelids are closed and disappearing when muscular contraction ceases.

Curschman and Loewi have observed that in a considerable percentage of cases of Graves' disease, the installation of *adrenalin* results in *mydriasis.*

Curschman (quoted by McCarrison) notes that in many instances the eyes present the phenomenon just the *reverse of the Argyll Robertson pupil, i.e.,* there is reaction to light, but not to convergence.

Ophthalmoscopic Changes.—These are not marked or typical. There may be a dilatation of the arterial vessels, their caliber becoming equal to that of the veins. Arterial pulsation is frequently discernible (Becker).

Optic Atrophy.—This may occur as a late sequel.

Vision.—Although not materially affected in early hyperthyroidism, vision may be altered as the disease progresses. In addition to corneal ulcers and conjunctivitis interfering with vision, the weakness of the ocular muscles as part of the general muscular weakness, adds to the difficulty. All these, with the occasional deficiency of convergence and sluggishness of pupillary activity, result in impairment of accommodation, rendering it imperative that the patient's eyes be refracted to conserve nervous energy.

The Nervous System in Exophthalmic Goiter

That there is no Graves' disease without subjective and objective circulatory phenomena has been stated; we might here add that the same is true of the nervous phenomena. Tremor, change in temperament and disposition, "nervousness" now asserting itself as hysteria, now as neurasthenia, again as melancholia, and rarely as insanity—one or more of these, especially the tremor and "nervousness,"—occur early in the disease, and often for a long time before other signs and symptoms significant of exophthalmic goiter appear. Let us consider a few of the nervous symptoms in the order of their diagnostic importance:

Tremor.—As this is considered one of the four cardinal symptoms of exophthalmic goiter, it is meet that we discuss the subject in some detail.

A tremor is a quivering or trembling occurring especially in the extremities. It is a kind of clonic spasm affecting a single group or many groups of muscles. According to G. R. Butler, a muscle is physiologically maintained in a condition of moderate tension by rhythmic impulses passing down from the motor cell bodies at the rate of approximately twelve per second. ''Ordinarily, the resulting muscular contractions are imperceptible, but if the strength of the impulse is increased, the muscular movements may be seen or felt as a tremor. If the rhythm and rate remain the same or eight to twelve per second, it is a fine tremor. If the disturbance is greater, every second impulse may be lacking, and coarse tremor, four to six, results.''

Tremor as a symptom of Graves's disease was described in the early history of the affection by Charcot and Marie. Though in the great majority of cases it is objective, this symptom may at times be subjective also, the patient stating that she feels herself ''trembling all over,'' more so during physical and mental activity and excitement than during rest.

The tremor of exophthalmic goiter is of the ''intention'' type. It is fine and involuntary, occurring about eight to twelve to the second. It is elicited by having the patient extend the arms and outstretch the fingers. In addition to this method, the subject may be given a tumblerful of water and requested to hold it a moment, then carry it slowly to the mouth. As the glass approaches the lips, it will begin to vibrate, and if full, some of the water will be spilt. In examining for tremor of the toes, the method of hyperextending them is employed as for the fingers.

Tremor is one of the earliest manifestations expressive of a hyperactive thyroid. It is not too much to say that if every patient complaining of vague functional disorders were made to stretch out the fingers to determine the presence of this symptom and then the rate of the heart observed, we would find more cases of incipient exophthalmic goiter, presenting two early cardinal symptoms—tachycardia and tremor—than ever before. Thus we would have a larger number of early curable cases and a much reduced number of late cases or human wrecks. A combination of tremor and palpitation, with a heart rate continuously ten or more above normal even while at rest, had better be managed as a case of early Graves' disease. Such a patient will recover far more rapidly than one who already presents exophthalmos and goiter.

Tremor is, in my experience at least, almost always present in this disease. Its intensity and distribution vary widely. It may occur in one finger only, or in two or more of one hand. Usually it occurs in all or nearly all the fingers of the patient, and occasionally also in the toes of one or both feet. In many cases, tremor of the protruded tongne will be seen. At times we observe a tremor of the eyelids (Rosenbach's sign). In a small percentage of cases, there is a fibrillary muscular tremor all over the body. This latter must not be confused with the throbbing of the head and trunk occurring synchronously with the cycles of a markedly hypertrophied and excited heart.

In order to differentiate between the various kinds of tremor seen in clinical work, we ask ourselves: What are the varieties of tremor and under what conditions does this symptom occur?

Tremors are of three kinds:

(*a*) The "intention" tremor which occurs only during voluntary movement and which is characteristic of hyperthyroidism.

(*b*) Passive tremor or that which ceases or diminishes after voluntary movement.

(*c*) That which is constant and is increased by voluntary movement.

A temporary tremor is commonly seen in the presence of *emotional excitement* especially in those of nervous temperament, *e.g.*, shock, extreme anxiety, fright, worry, etc. It also occurs after violent or long-continued exercise.

The tremor of the various *intoxications*, *i.e.*, lead, arsenic, mercury, alcohol, tobacco, tea and coffee, and after the drug is stopped in opium, morphine, and cocaine fiends, are at first "intention" tremors, but as time goes on the tremor becomes constant, and with the advance of the toxic process, muscular coordination becomes more and more difficult. The tremor is fine, rapid, regular, and rhythmical, and is traceable to the proper cause by the absence of other pathognomonic signs of hyperthyroidism in the presence of a distinctive history leading to the correct conclusion. The various types of intoxications present in themselves specific signs and symptoms which are not essential to our purpose in this work.

Any organic abnormality of the nervous system is apt to give rise to a tremor of varying type or degree. These must be judged on the merits of the case; the clinician who has a fair knowledge of the diseases of the nervous system and is well versed in the various manifestations of Graves' disease will not be troubled by the pitfalls which stand in the way of the superficial observer.

The tremor of *paralysis agitans* is at once distinguishable from all other tremors by the fact that it is of the slow, "bread-crumbling" variety, easing for a while during voluntary movements. The slow, monotonous speech, expressionless countenance, peculiar gait and posture on walking, clinch the diagnosis.

The tremor of *hysteria* is usually fine and rapid, but may be moderately slow and coarse. The rhythm, regularity, and even the very presence of the tremor are inconstant; these vary with the moods and whims of the patient. Such a tremor need not perturb us in diagnosis, for here again the absence of the characteristic signs and symptoms of exophthalmic goiter and a clear history will aid us in our proper deductions. We must here bear in mind that many cases of hysteria present a history of palpitation, show intermittent tachycardia of moderate severity, and at times there is even slight exophthalmos.

The tremor often present in *neurasthenia* resembles that of hysteria, excepting that it is apt to be more regular and rhythmical, and is more promptly amenable to treatment.

The tremor of *senility* need not detain us. It is rapid and is at first "intention" in type, becoming constant as the process advances. It begins in the hands, gradually extending to the neck muscles, the head and the rest of the body. The diagnosis is readily made by the absence of other cardinal features of hyperthyroidism and the presence of advanced years, arteriosclerosis, high blood pressure and other signs of senility.

The tremor sometimes *inherited* through a long line of descendants resembles the senile tremor. This is easily distinguished from that of hyperthyroidism by the history, the fact that it has existed as long as the patient can remember, and that there are no evidences of Graves' disease.

The tremor of *multiple sclerosis* is persistently "intention" in type. It is slow and irregular and is associated with the other cardinal symptoms of the disease, namely, the muscular weakness with rigidity, exaggerated reflexes, disordered speech, nystagmus, vertigo, epileptiform and apoplectiform attacks, and mental deficiency.

The movements characterizing the subject of *chorea* are not tremors, but merely sudden, nonpurposive, incoordinate movements of various groups of muscles, which movements cease during voluntary effort. They are nonrhythmical and diminish or cease when the patient is in a state of concentrated attention or sleep. These cases, as a rule, are seen in young people. There is nothing in a case of this sort resembling the symptoms of Graves' disease.

I have often noticed a rhythmical nodding of the head and often, in fact, of the whole body, the rate corresponding to the number of cardiac cycles per minute in the tachycardia of exophthalmic goiter. Though this may in a very broad sense be considered as a tremor of the head and body, strictly speaking it is not so, since it is not of nervous, but of cardiac origin. The heart beating at the rate of from 110 to 160 per minute labors so strenuously that it soon becomes enormously hypertrophied (which immediately precedes dilatation and in severe cases, loss of compensation), so that this organ, acting as a huge, excited pump within the chest takes with it, as it were, the head, shoulders, body, and all, during each contraction.

Since in Graves' disease the symptoms are not always present in syndrome, but frequently one symptom, such as enlarged thyroid or nervousness or tachycardia, may precede the others and exist alone for some time, the question arises: Is this applicable to the tremor? Does the tremor ever precede the other evidences of Graves' disease, existing alone for weeks or months as a precursor to the other cardinal symptoms? This can not be answered with any degree of definiteness, excepting to say that, strictly speaking, the tremor *alone* probably does not precede the other manifestations. It may apparently precede, but in reality it is coexistent with some heart-hurry, palpitation during exertion or excitation, nervousness, and possibly the change of disposition of the patient. These symptoms may occur so insidiously that even the patient will not be aware of their presence, but might complain casually of "nervousness" or "rundown system."

Temperament and Disposition.—The patient is easily excited; the slightest noise, a sudden call, a slight peal of thunder, and the exophthalmos is markedly accentuated, the heart thumps away at a terrific rate, and the features become distressed and anxious. These patients are easily aroused to the extreme of almost any emotion; fright, anxiety, terror, suspicion, anger, may alternate with surprising rapidity and upon the most trivial provocation.

In obtaining the history of a male patient suffering with early exophthalmic goiter, the wife made the following significant remarks: "George has not been himself the last several weeks—I can't make him out. He acts queerly—somewhat different from his usual behavior. He does things he never did before; he says things I least expect from him. He becomes impatient and excited for no reason and cries like a baby without the least cause. I try to be as good as possible to him, but I can't make him out. I don't understand him any more. Do you think he'll lose his mind, doctor, or is he just very nervous?" This is a common situation, whether it be found in male or female, married or single. The relatives and friends can not "make the patient out," or to be more lucid, there is a diminished or absence of "understanding" between the patient and those about, because of the quickening, exciting effect of the excessive quantity of thyroid hormone irritating the cerebrospinal axis. Barker states: "One of my patients gradually became so irritable and violent that his wife, not knowing the cause, had him before a magistrate and bound over to keep the peace. Another became so anxious and disturbed that she lost confidence in herself and had to be sent temporarily to a closed institution pending the passing of the psychosis."

The emaciation, the staring eyes and the departure from the normal of the subject's manners, all conspire to deserve for the patient the title "queer" from those about him. This patient, though formerly capable of sustained physical and mental effort, is now quite different. The sharpened intellect and drive of determination to accomplish, seen in such a subject remind one of the spur to action from the use of moderately large doses of caffeine, but in thyroid toxemia the individual tires of the subject in hand more easily. He is enthusiastic, intense, and eager for brief periods only. Tastes and desires vacillate with unusual rapidity. The marked lack of perseverance, shiftlessness, a tendency to hop from relevant to irrelevant thoughts, expressions and actions, characterize the day's roster. When evening comes sleep is not a cheerful prospect, and when the patient finally retires, the night is a partial or complete torture. The insomnia and tossing about in bed, the sweating and throbbing of the heart, especially when lying on the left side, make the break of day an eager anticipation. The patient, though glad to leave bed, arises in the morning feeling "all in"—tired, weary, gloomy, irritable and totally unfit for work or society. Thus the next day and night are spent in similar fashion, and so on through weeks and months. Is it any wonder that the nervous system sooner or later "breaks" under this strain, resulting in mania and dementia?

At times the reverse is seen; instead of evincing an overly alert, hyperactive demeanor, the patient is morose, moody and melancholy, fretting the time away. This may be due to the result of *overstimulation* of the brain cells by the thyroid toxemia, for it is a known biological fact that cellular overstimulation leads to depression. The patient is physically and mentally depressed and apathetic. The mind, left to itself, soon reverts to such pathways as anxiety, apprehension, phobias, obsessions, persecutory delusions, unwarranted suspicions, and hallucinations of varying degrees of importance.

Periods of extreme anger, rage, stubbornness, hatred of things and persons formerly loved and cherished, and even suicidal and homicidal tendencies are apt to occur in either of the above types of cases.

In a small percentage of cases, periods of stimulation or exuberance alternate with periods of depression, so that the aforementioned characteristics may exist at different times in the same patient—a veritable chaos of emotional tendencies.

Miscellaneous Nervous Phenomena.—In recent years, observers have noted an interesting relationship between a certain percentage of cases of *epilepsy* and disorders of the thyroid. H. R. Harrower believes that the thyroid gland, because of its intimate relation to detoxication and to metabolism in general, should be considered as a possible factor in the etiology of epilepsy. In cases in which evidence of thyroid deficiency is noted, thyroid therapy can be expected to act as an effective adjuvant to other measures directed toward the epilepsy.

Drysdale remarks that a considerable number of cases of epilepsy present symptoms of endocrine disorder. These stand out more or less prominently, and it is quite probable that the internal secretions exercise some relationship to this disease. Among the suggestions as to treatment, Drysdale includes the administration of thyroid extract and states that in some instances this "has true therapeutic worth."

Headache, variable in location, most often frontal, is common and due to a variety of obvious causes. At times attacks of typical *migraine* of varying intensity and duration occur.

Insomnia is almost the rule and differs in intensity with exigencies of the case. The throbbing of the heart and blood vessels, the drenching sweats, irritability of the bladder, and the general high-tensioned state of the psychic centers—all of these rob the subject of the night's rest and cause the patient to dread the close of day. Insomnia is an early symptom, and it may be said in passing that the tendency to sound, refreshing sleep is excellent evidence of successful treatment and a beginning restoration to health.

Pains in various parts of the body are commonly experienced, resembling in character those occurring in diabetes mellitus. A feeling of weakness in the knees and calves of the legs is often early and distressing. These pains are often truly rheumatic in nature, but care must be exercised in making deductions.

Chorea may precede or accompany either casually or exist coincidentally with exophthalmic goiter. A case of this sort merely complicates matters somewhat, but careful observation will yield the diagnosis.

Reflexes are usually exaggerated, though they may be normal, and rarely, in the depressed patient, subnormal.

Psychoses.—Typical evidences of *neurasthenia* and *hysteria* are commonly seen in exophthalmic goiter and need not be enumerated here. The symptoms may occur at different times with respect to the time of appearance of unmistakable signs of exophthalmic goiter. Neurasthenia, hysteria or hysteroneurasthenia may apparently (*a*) precede the Basedowian syndrome by some weeks or months; (*b*) they may appear concomitantly with one or more cardinal signs of the syndrome; (*c*) they may occur weeks or months after the diagnosis of Basedow's disease has been definitely made. The situation is well elucidated by Tanzi: "Cases of exophthalmic goiter which present hysterical phenomena should be regarded as latent hysteria brought to the surface by exophthalmic goiter. It is the hyperthyroidism which evokes the syndrome. Because of the associated symptoms of exophthalmic goiter, we can clearly determine that it is the thyroid toxin which has initiated the hysteria just as it initiates the sensitiveness, the depression, and the anxiety which are common manifestations of the thyroid disease. There may have been a susceptibility to acquired hysteria, but this does not negative the fact that the hysteria has been manifested through the external determinant—the thyroid toxin."

Insanity and exophthalmic goiter have very often been observed in the same patient. Arsimoles and Legrand have observed a type of mental disorder similar to manic-depressive insanity, due directly to thyroid intoxication. Kappenburg, in his paper on the relation of goiter to mental conditions, reports that twenty per cent of the 561 persons with goiter at the Utrecht Hospital presented more or less pronounced mental impairment, while only 4.4 per cent among 437 other inmates showed anything of the kind. Of the 11 goiter cases referred to nearly all were of the manic-depressive or melancholia types of psychosis, while this was true of only 1.1 per cent among the others. He concludes that the thyroid gland seems to be affected more than other endocrine organs by emotional influences. It is the "*glande de l'émotion*" as it has been called. He compares the various theories as to the pathogenic influence of the thyroid and its connection with psychic depression. He declares that such an influence exists, and the figures he presents sustain this assumption.

That the thyroid is frequently found abnormal in structure and function in the adolescent and adult insane is conceded by nearly all clinicians. Dementia, mania, and the related psychoses are commonly seen during the height of the course of exophthalmic goiter. On the other hand, numerous instances of insanity have been observed in which the syndrome of Graves' disease became apparently superimposed. It is sometimes difficult to decide which is the cause and which the effect in such cases.

In concluding this brief survey of the nervous symptoms, it must be remarked that an inherited tendency to a departure from the normal of the accepted standard of mental poise is very prominent in many Basedowian patients, especially in those whose psychical disturbances are most marked. The thyroid toxemia (as indeed all other toxemias) attacks the individual most sharply in the most vulnerable parts, and if this be the psychic centers, the symptoms will be correspondingly accentuated.

The Gastrointestinal Tract in Exophthalmic Goiter

The gastrointestinal phenomena, especially the nausea, vomiting, abdominal discomfort and diarrhea, in the presence of the markedly increased oxidation of the bodily tissues, are responsible for the great wasting of the body so characteristic of exophthalmic goiter.

The teeth and gums are at times in poor condition, which status may bear etiologically on the disease. It has been observed that the correction of decayed teeth, especially the cure of pyorrhea alveolaris, has aided materially in the restoration to health of a Basedowian subject.

Dysphagia, usually in slight degree, is rarely encountered as a pressure symptom, but is eminently more often met with in the "Basedowified" or secondary forms of the disease.

The saliva is at times diminished, but an increased output is more commonly seen. Occasionally the sialorrhea is quite as troublesome as in the extreme cases seen by obstetricians in pregnancy.

Anorexia, though common, is not a constant symptom. Some patients possess a normal appetite, while an occasional sufferer with hyperthyroidism will have the ravenous appetite characteristic of diabetes mellitus, in spite of which there is gradual loss of weight and strength.

Nausea and vomiting simulating nervous dyspepsia are quite commonly seen and may be attributed to the nervous instability. During an attack of acute hyperthyroidism, and in the advanced stage of the usual chronic type of the disease, the vomiting, partially caused by gastric achylia, may become so severe as to precipitate a fatal termination.

The various manifestations of nervous dyspepsia coupled with a gradual loss of weight and strength, may precede for a variable time the cardinal symptoms of exophthalmic goiter. Usually these symptoms coexist with a fair degree of constancy. There may be marked hyperchlorhydria, but at times there is hypochlorhydria.

Gastrospasm, pylorospasm and their several manifestations, gastralgia, and almost any combination of abdominal symptoms may be presented by these patients. In this connection it is interesting to quote Solomon Solis-Cohen: "Sometimes, indeed, the visceral symptoms are so pronounced that a not unjustifiable diagnosis of inflammation or degenerative lesion is made; for example, appendicitis, gastric ulcer, nephritis. Cases simulating pretty closely the symptomatology of gall stone or kidney stone may occur, and give the physician as well as the patient great anxiety. I have myself counseled exploration or operation in order to remove doubt in one case of simulated hepatic colic and two cases of simulated appendicitis; and I may add that the sections, while negating the diagnosis of inflammation or calculus, at least permanently relieved otherwise intractable symptoms. Sometimes actual organic lesion, of the same kind as the commonly simulated affections, *e.g.*, gastric ulcer, appendicitis, nephritis, may develop in an angioneurotic subject, and such cases are doubly difficult. Displacements of organs (visceral ptoses) are not uncommon, and while these conditions have their own special symptomatology, relieved by appropriate, perhaps even surgical, treatment, they do not constitute the entire case."

Constipation, more often diarrhea, occasionally a periodic alternation of the two, are important features. The diarrhea is at times very severe, intractable, and stubborn to remedial measures, in rare instances becoming alarming with the onset of intestinal hemorrhage. The flooding from the bowel may intermit, giving way to a degree of constipation, or it may continue on to a fatal termination. A large percentage of cases, however, are not troubled by intestinal difficulties to any great extent.

The character of the feces varies widely. They may be normal,—or present traces or quantities of blood. Often one may observe the features of pancreatic and biliary disease, *i.e.*, clay-colored stools containing fat and undigested meat fibers.

The Cutaneous Symptoms in Exophthalmic Goiter

The skin in hyperthyroidism is a very interesting study and presents phenomena in direct contrast to those of hypothyroidism. It is thin and moist to the touch, and if a finger is kept in close contact with any part of the body surface for a few seconds, with moderate pressure, its removal will be followed by an area of pallor corresponding to the finger mark, which in a few seconds fades away, giving rise to a pinkish hue which remains for from a fraction of a minute to a minute or more.

The skin in exophthalmic goiter is in the majority of patients of dusky, plethoric hue and somewhat greasy from the excessive secretion. Though there may be a degree of secondary anemia or chloroanemia, this is not evident on the surface because of the partial vasomotor paralysis of the peripheral arterioles. Of course, areas of edema,—the ankles, legs or elsewhere, due to cardiac failure, will appear pale and doughy, and pit on pressure. This must not be confused with the pale, doughy skin of myxedema, which does *not* pit on pressure.

Pigmentation is commonly seen, and as elsewhere observed, suggests the interrelationship of the thyroid gland with the suprarenals. The percentage of cases in which pigmentation is found varies with the observation of different authors: Denton Cardew claims to have observed it in 70 per cent of cases, while West observed it in only 16 per cent of cases. Sainton and Fayolle have seen it in 25 per cent of their series of cases and describe four principal varieties of this pigmentation: (1) localized pigmentation; (2) more or less diffuse pigmentation; (3) Addisonian melanoderma with pigmentation of the mucous membranes, and (4) generalized pigmentation of Addisonian type without discoloration of the mucous membranes. The localized form of pigmentation shows a predilection for the face. It consists sometimes of small brown spots somewhat larger than common nevi; in other instances of brown patches generally extending in the region of the neck. The appearance presented is that of the chloasmic mask of pregnancy; indeed, it is not improbable that these two conditions arise in the same manner.

Hyperidrosis, or excessive sweating, is common and very annoying to the patient, and gives rise to the increased electric conductivity of the skin (Vigouroux). This sweating occurring especially at night, in the presence of emaciation, weakness, slight rise in temperature, dyspnea and diminished respiratory expansion may lead to a tentative diagnosis of pulmonary tuberculosis. In addition, this symptom must not be confused with the sweating seen in the following conditions: the crisis of fevers, marked physical and mental strain, great weakness and collapse, the debility of convalescence, infections and septic conditions, and the action of diaphoretics. In a letter to the editor of the "Lancet," R. J. Cyriax draws attention to a peculiarity exhibited by some patients suffering from exophthalmic goiter—namely, a tendency to wash their hands with a frequency out of all proportion to necessity. He attributes this phenomenon to hyperidrosis of the hands, especially of the palms, in a certain number of cases; however, the statement is made that these symptoms occur in cases in which there is no excessive sweating of the hands. The patients complain that their hands always feel dirty. In this latter type it is possible that these individuals are suffering from a neurosis. The author attaches importance to this symptom as it sometimes appears in comparatively early cases. He reports seven cases of exophthalmic goiter—all women —in which this symptom occurred.

Dermographia is usually present in exophthalmic goiter, and is considered a state of *vasomotor ataxia* by Solomon Solis-Cohen. With a blunt-pointed probe, or the edge of a silver coin, or even the finger nail, markings or letters are traced out on the patient's skin—usually the back, employing moderate pressure. Following the immediate pallor of the tracings, there will be a reddening within eight to ten seconds, which, reaching the maximum hue within a half minute, begins to fade ten or fifteen seconds later. The promptness of occurrence and degree of intensity of the dermographic markings vary with the degree of thyroid toxemia and with other unknown factors.

Kahane describes a form of vasomotor irritability which he terms "galvanopalpation." "The negative electrode is attached to some distant portion of the body. The positive electrode, which should be sharp, is then lightly applied to the skin over the thyroid gland. If the pain reaction is intense and there is a marked redness which persists for a long time, the thyroid gland is considered to be functioning to excess. It is necessary, for comparative purposes, to use always a galvanic battery of standard strength."

Erythematous areas or blotches are commonly seen, due also to the vasomotor instability.

Pruritus of variable degree, often as troublesome as that occurring in diabetes mellitus, is occasionally encountered.

Urticaria is observed, especially where the gastrointestinal symptoms are severe.

Scleroderma usually more or less circumscribed, has been observed in several instances. The reports of scleroderma in exophthalmic goiter are becoming more numerous in recent years.

Of special diagnostic importance is the fine pinpoint petechiæ, most often occurring over the front and upper portion of the chest.

Angioneurotic edema is occasionally observed in patients suffering with exophthalmic goiter and suggests a common vasomotor neurotic etiology.

The temperature of the skin in subjects of exophthalmic goiter is frequently elevated to one or more degrees above normal.

Peripheral stimuli are more rapidly conducted, more acutely and intensely translated, and the responses are exaggerated.

The Goetsch cutaneous reaction to adrenalin is described under "diagnostic tests."

Indicating loss of occipitofrontalis control, the forehead is smoother than in health, with failure of the forehead to wrinkle on looking up (Joffroy).

Marked diminution in cutaneous resistance to electrical currents is an almost constant symptom (Charcot).

The hair, including the eyebrows and lashes, may become brittle and fall out.

The nails may become brittle and break.

The Respiratory System in Exophthalmic Goiter

Nasal obstruction, due to chronic rhinitis, polyps or adenoids, may be discovered, and is often of etiologic importance. Cases have been reported of cure following the removal of polyps and adenoids. The same may be remarked of enlarged diseased tonsils.

Diminished respiratory expansion and an increased respiratory rate are almost the rule in Graves' disease and are partly responsible for the dyspnea so commonly complained of by these patients. Associated with this as cause, effect, or both, is observed a flattening of the anteroposterior diameter of the chest which, with the emaciation, approximates in type the phthisinoid or even the phthistical chest. What produces this dimished expansion, this gasping on slightest exertion? Very likely a combination of these factors: (*a*) increased cellular oxidation; (*b*) weakness of muscles of respiration; (*c*) excitation of respiratory center by the toxemia; (*d*) the presence of active or latent phthisis.

Alteration of voice, hoarseness and cough are not uncommonly observed in exophthalmic goiter. These symptoms are usually due to a compression and irritation of the inferior laryngeal nerve by the enlarged thyroid, irritation and compression of the muscles about the larynx and of the vocal cords, or they may be produced by a preexisting primary morbid condition of the throat or larynx. If cough is due to a coexisting phthisis, it may be associated with expectoration of variable character. An enlarged thymus is rarely responsible for cough and paroxysmal attacks of choking. Rarely, in cases of accentuated nervous phenomena, these symptoms may be of hysterical origin.

Much has been said of the frequent association of tuberculosis, especially of the lungs, with exophthalmic goiter. Knopf, Bialokur (see "Pathogenesis") and many others have been impressed with the apparent intimacy existing between the two diseases. Caro found signs of an apical process, probably of tuberculous origin, in 210 out of 486 men with thyroid symptoms, and Schinzinger found a tendency to goiter in 355 out of 521 tuberculous patients. Only 191 of these 355 patients had symptoms suggesting exophthalmic goiter. Swan, in his series of 50 cases, states that 2 had definite evidence of pulmonary tuberculosis, 6 had suspicious apices, and 4 had chronic pleurisy. Santa Maria describes a case in which the vagotonic hyperthyroidism suggested exophthalmic goiter, but unmistakable signs of apical tuberculosis disclosed its toxic origin from the tuberculous toxins. Under treatment of the tuberculosis, the apex cleared up and with this all the thyroid symptoms disappeared. In some cases of pure exophthalmic goiter, the writer has witnessed a spasmodic cough suggesting tuberculosis, of purely vagotonic origin, as also in some cases of simple poisoning from thyroidin. Hypothyroidism may accompany tuberculosis, and thyroid treatment may effectually supplement treatment of the tuberculosis, which without it may fail of success.

The rise in temperature, persistent sweating, diminished respiratory expansion, weakness, and loss of weight, frequently lead doctor and patient to suspect phthisis. The following tabulation will assist in differentiating, though as has already been mentioned, the two conditions sometimes exist in the same patient.

Pulmonary Tuberculosis	*Exophthalmic Goiter*
(*a*) No thyroid fullness, tremor, or exophthalmos.	Thyroid fullness, tremor and exophthalmos.
(*b*) Usually a history of exposure to the disease directly or indirectly; or a tuberculous family history.	Not so. Frequently a history of nervous shock or neuropathic tendency.
(*c*) Cough, expectoration, vague chest pains and often Koch's bacillus in the sputum. Tuberculin reaction. Characteristic physical signs over the lungs.	Not so.
(*d*) X-ray examination reveals pulmonary lesions.	X-ray examination may reveal enlarged thymus and dilated heart.

Asthma, considered by some as a form of vasomotor neurosis manifestation is looked upon as somewhat related to the Basedowian syndrome. Hofbauer believes that asthma may be a manifestation of Basedow's disease. Curschman (quoted by O. H. Brown) reports two cases of Basedow's disease that also suffered with asthma. He believes that asthma may result from a vagotonia or a sympatheticotonia, both of which may be manifestations of the Basedow syndrome. Though we do not often meet with Graves' disease and asthma in the same patient, these suggestions should give us food for thought.

The Genitourinary Tract in Exophthalmic Goiter

As we have seen in the chapters on "Physiology and Pathogenesis," the functions of the thyroid gland are intimately related to those of the organs of reproduction,—and diseases of the thyroid, especially alterations in its functions are commonly associated with abnormalities in structure and function of the genital organs.

In exophthalmic goiter the menstruation may undergo marked variations from the normal. There is occasionally a cessation of this function for a variable length of time. This may occur particularly in instances of marked emaciation and asthenia, the menstrual cessation being an effort on the part of nature to conserve the bodily forces. The menstruation may be irregular in occurrence, duration, and quantity,—now on time, now too soon, again delayed, at one time diminished, at another very profuse and weakening. Since in exophthalmic goiter there is diminished coagulability and viscosity of the blood at times approaching hemophilia in character, menstruation may in isolated cases become so profuse and protracted as to occasion much concern and necessitate corrective therapeutic measures.

The sexual *libido* and *potentia* vary in different cases and vacillate at different times in the same patient. The sexual instinct and drive are usually diminished, sometimes almost suppressed by the thyroid toxemia. Occasionally, however, and I have observed it especially in the male, there may occur an annual increase in the family during the course of the affection and immediately following cure.

The affect of hyperthyroidism on the fecundity of the female is a subject upon which many observers differ in their opinions. Some claim that thyroid toxemia hinders pregnancy, and that when this *does* occur, the patient is likely to abort. Others claim that fecundity is increased by hyperthyroidism. Still others believe that, pregnancy having occurred, the thyroid hyperactivity is increased, and that the Basedowian status is intensified during the course of the disease. A small percentage of investigators believe that pregnancy temporarily improves Graves' disease, but that the disease becomes aggravated after childbirth. Since no two opinions agree in principle, I feel it incumbent upon me to offer my own conclusions on the subject: Pregnancy is not hindered by hyperthyroidism; there is a tendency to abort, but this is not to an alarming degree; delivery is apt to be followed by postpartum hemorrhage. I have recently had under my care 2 cases of exophthalmic goiter in pregnant women who were delivered of healthy, robust infants. Everything was normal excepting the strong tendency to excessive bleeding. In one of the cases, the postpartum hemorrhage necessitated packing the uterus. These patients were under careful therapeutic treatment for some time preceding and during gestation. At this writing, their Basedowian syndromes have disappeared, and the children are in perfect health. Now a few words of warning to the general practitioner when attending a subject of hyperthyroidism in labor: (*a*) do not urge the patient to strongly bear down, as this may cause a marked increase in the size of the goiter and in the degree of exophthalmos; (*b*) when the presenting part approaches the perineum, the use of a few whiffs of chloroform combined with an injection of pituitrin or low forceps delivery are laudable procedures and serve to reduce shock and overcome the objections under (*a*); (*c*) after the placenta comes away, administer a double dose of ergot and *do not leave the patient* for at least two hours after delivery is completed.

Of course, there is a degree of physiologic thyroid hyperactivity during pregnancy which must not be construed as abnormal. For some reason, in some instances this increase persists and after delivery we are confronted with a case of Graves' disease.

The gynecologic lesions often found to coexist with the Basedowian syndrome have given rise to the assumption that they are causally related to the thyroid abnormalities in these cases. This is apparently proved by the many instances brought to our attention in which a pelvic operation with the removal of the offending lesions has cured the exophthalmic goiter. Moreover, the correction of certain abnormalities of the uterus or adnexa by x-ray exposures has also resulted in the amelioration of the symptoms of exophthalmic goiter. In these cases, then, the syndrome of Graves' disease is associated with the pain, menstrual disturbances and reflex phenomena characteristic of the existing pelvic lesion.

Polyuria and the frequency of micturition often seen in Graves' disease is a troublesome symptom. It not only increases the diurnal discomfort of the patient, but is an important element in the production of insomnia. One of my male patients was compelled to rise as often as ten or twelve times every night to relieve the bladder. The cause of this symptom is not clear, but it is probably due to several factors, among which may be mentioned the increased tissue oxidation, the polydipsia, the hyperglycemia, the irritability of the kidneys, and the neurosis of the bladder. Polyuria may for weeks or months be a forerunner of exophthalmic goiter. In the presence of a coexisting parenchymatous nephritis, the reverse will be the case, urination will be scanty and infrequent; but this is rarely met with in exophthalmic goiter.

Glycosuria in varying degree is commonly seen in exophthalmic goiter and may be experimentally produced in normal persons by thyroid administration. This is due to the carbohydrate intolerance probably resulting from the depressing effect exerted by the thyroid toxemia on the pancreatic functions. The greater the severity of the thyroid toxemia the greater the glycosuria until, in advanced cases, we are confronted with a symptom-complex approximating in character a full-fledged case of diabetes mellitus as a complicating or intercurrent affection. When this occurs our treatment must be changed accordingly: the diet must be restricted in carbohydrates, or starchy foods must be withdrawn for a while. In some, a frankly outspoken condition of diabetes mellitus is observed to precede for a time, appear concomitantly with or some time after the onset of the exophthalmic goiter.

Albuminuria (usually transient) is often present and is due to a coexisting nephritis, an irritation of the kidneys by the oversupply of thyroid substance in the blood, the passive congestion consequent upon cardiac incompetency, or to a combination of these causes. It rarely assumes alarming proportions and is occasionally accompanied by hyaline and granular casts.

The accelerated total metabolism in hyperthyroidism gives rise to an increase in the output of the urea nitrogen, total nitrogen, uric acid and the phosphates in the urine.

CHAPTER VI

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The cardinal symptoms are enlarged thyroid, exophthalmos, tremor of the outstretched hands and tachycardia. In the presence of these four, the diagnosis is simple, and the case is merely one of therapeusis. But a clear-cut combination of all cardinal symptoms in a given patient is not the rule, to say the least, and the diagnosis of Graves' disease is often fraught with difficulties. In many cases the patient is questioned and examined with a view to the discovery of some other more common morbid condition, and hyperthyroidism is not thought of. Though exophthalmos and enlarged thyroid put the diagnostician immediately on his guard, these symptoms in early cases are either entirely absent or so slight as to be entirely overlooked. With regard to the thyroid, the difficulty is increased by the question as to whether or not a moderate enlargement of the thyroid is physiologic only, and brought about by menstruation or pregnancy. Though usually the last to appear, exophthalmos is, in rare cases, the only feature present for a long time. But cardiovascular symptoms usually occur early, and a subject of hyperthyroidism is rarely if ever free from continuous or spasmodic occurrence of palpitation, tachycardia or arrhythmia.

The unaccountable, persistent tachycardia, the palpitation and the drenching night sweats unassociated with the physical signs of tuberculosis are always highly significant. Persistently increased frequency of urination and polyuria, especially in a young woman of highly neurotic temperament who complains of paroxysmal palpitation and intractable diarrhea must be considered at least suspicious of Graves' disease, as these symptoms are frequently forerunners of a typical development of hyperthyroidism. In the average case, the most constant symptoms in the order of importance are referable to the circulatory and nervous systems. The patient presents an afebrile tachycardia with subjective circulatory phenomena concomitantly with a kind of "nervousness" which is not at all comparable to that often seen in otherwise normal persons, and to which all flesh is heir at certain times. The nervousness of hyperthyroidism differs in that there is an actual degree of change in disposition and temperament of the individual, which is persistent and accompanied by a fine tremor of the outstretched fingers and sometimes of the toes, which tremor may at first affect but one, two, or three fingers; there is slight fullness of the neck, which may not be discernible on inspection or even palpation, but is noticeable only when the patient finds the usual size collar too small; and there is the bulging of the eyes or exophthalmos, the sign which is usually last in order of appearance. This latter may in a large percentage of cases appear as a stare recognized by members of the family, which is in reality the beginning of the exophthalmic process, and sooner or later the eyes distinctly bulge forward, giving the patient's features an uncanny expression, which frequently tends to frighten those of his friends who have not seen him for a long time. In addition, the feeling of muscular weakness not benefited by rest, but on the contrary, an intensification of the fatigue on arising in the morning, a perpetual, distressing sense of being "all in" especially when initiative and effort are required, an inability to apply the usual physical and mental forces for more than a brief while at a time—the vacillation of aspiration and determination, or occasionally their absence—all these, accompanied by a gradual and persistent loss in weight, mean hyperthyroidism, and the sooner the rational treatment is instituted the better.

Since exophthalmic goiter in its early stages may resemble many other conditions more commonly encountered in the practice of medicine, and since in its advanced stages the disease is apt to be atypical and lead to pitfalls in diagnosis, it behooves us to bear in mind the most usual conditions with which it may be confused and the signs and symptoms of their differentiation. The following conditions are to be differentiated from Graves' disease:

Simple or Nontoxic Goiter is differentiated from the primary hyperplastic goiter in the section on "The Thyroid Gland."

Secondary or "Basedowified" goiter is also differentiated from the primary form in the same section.

Neurasthenia may be the forerunner of exophthalmic goiter, or it may accompany the disease; as a general rule the two conditions have many things in common, and when it becomes a question of differentiating between a primary, unalloyed case of neurasthenia and one of Graves' disease, we are often confronted with a difficult problem. In this connection Crile's views are interesting: "Worry, fear, grief, infections, overwork, autointoxication, etc., are the common exciting causes of exophthalmic goiter. Any one of these excitants may just as readily cause neurasthenia, cardiovascular disease, cardiorenal disease or diabetes. Let us consider that protean disease neurasthenia. It is produced by environmental stimuli that give rise to exophthalmic goiter; it is relieved by rest, by controlling work, by eliminating worry, infection, autointoxication, etc. If the exciting causes of exophthalmic goiter and neurasthenia * * * are practically identical, what then is the essential difference between neurasthenia and exophthalmic goiter? In many cases of pathologic drive the diagnosis by one physician will be light exophthalmic goiter, by another neurasthenia. It may be compared to the distinction between wealth and riches,—they are apparently varying degrees of similar processes." But we must remember that though some instances of "light exophthalmic goiter" may be improved by a treatment outlined for neurasthenia, it is a sad, often fatal mistake, to fail to differentiate these two conditions in diagnosis and treatment. To proceed a step farther in our views, it is not unreasonable to assume that in the future we may determine that all neurasthenics are really so because of some peculiar hormone disturbance of definite degree and character, to be differentiated from the hormone disturbance of Graves' disease. A careful history and an alertness in clinical and laboratory observation will serve to distinguish the two conditions in practically every case. We must here repeat that treatment for neurasthenia will, in the vast majority of cases, fail to cure a patient suffering with Graves' disease.

Hysteria and hysteroneurasthenia present almost the same problem. Here the two may precede each other or develop mutually into a symptom-complex in the same patient. The spells of crying on the slightest provocation, the stubbornness, the change in disposition and the varying likes and dislikes, the palpitation, tremor, and staring of the eyes are, of course, common to both hysteria and Graves' disease. But in primary uncomplicated cases the diagnosis should be apparent after a period of careful analysis of the history and symptomatology. The tachycardia of exophthalmic goiter is constant, awake or asleep; the tremor is constant and typical; the thyroid is full and tender; and the diagnostic eye signs are obtainable. This is not true of hysteria or of hysteroneurasthenia.

Nervous indigestion is only too often the diagnosis made in the early forms of exophthalmic goiter because of the nausea, vomiting, epigastric tenderness, pyrosis and general abdominal discomfort so often occurring as prominent symptoms in the Basedowian syndrome. Here a therapeutic regimen calculated to overcome the subjective symptoms fails and the medical attendant is perplexed as to what next to do for the patient. The difficulty is overcome by mere attention to *details* as above suggested, and the diagnosis will loom forth within a few weeks.

Pulmonary tuberculosis is frequently thought of in the presence of the gradual loss in weight, hyperidrosis, rise in temperature, weakness, diminished respiratory expansion and dyspnea. The differentiation is discussed under the "Respiratory System."

Paroxysmal tachycardia is differentiated in the section on the "Circulatory System."

Angina pectoris is rarely confused with hyperthyroidism. Although anginoid pains severe enough to resemble angina pectoris may occur in advanced cases of Graves' disease because of the tumultuous action of the heart, a state of unmistakable angina pectoris occurs so rarely that it need not give us much concern. It must be remembered that anginoid cardiac symptoms may occur through pressure on the thoracic vessels by an intrathoracic goiter as an evidence of the mechanical "goiter heart." In general, angina pectoris is excluded by the history of the usual etiologic factors, especially syphilis, alcoholism, and hereditary tendency to circulatory diseases; plumbism, rheumatism and the like, the presence of an abnormally high blood pressure, fibrosis of the blood vessels, the occurrence of the attacks in paroxysms with the sensation of impending death (the heart's rate often being quite normal during that time), and the absence of the cardinal symptoms of exophthalmic goiter.

Addison's disease may precede, accompany or follow exophthalmic goiter in isolated instances, and often this is so striking that we can not help being impressed with the apparent relationship between the two diseases and physiologic mutual dependency between the thyroid and the suprarenals. Moreover, one meets very often with ordinary or usual types of exophthalmic goiter presenting patches of pigmentation of undoubted adrenal origin. It is for these reasons that occasionally some difficulties arise in differentiating exophthalmic goiter from Addison's Disease, which are again overcome by a careful attention to details in the history, symptomatology, and laboratory data.

Symptomatic anemia is present in all cases of advanced Graves' disease resulting from the thyrotoxemia and its widespread effects on the vital body processes. Because of the vasomotor instability or *vasomotor ataxia,* the blood impoverishment may not be evident on inspection, the patient often appearing flushed. It is only by means of a blood analysis that we can determine the degree of anemia present. The conclusion that the patient is suffering from "anemia and a run down system" is not a rare occurrence in instances of early exophthalmic goiter and must be guarded against.

Septic endocarditis is sometimes thought of when the symptoms of hyperthyroidism are acute. In the presence of a frenzy or delirium, so to speak, of cardiac function, marked prostration, sweating, feverishness and great weakness, it becomes a rather difficult matter to rule out septic endocarditis. A careful history will usually reveal in the latter case the presence of a preexisting infection, such as acute articular rheumatism, lobar pneumonia, scarlet fever, typhoid, erysipelas, etc. There is marked pain over the abdomen and elsewhere, evidences of embolic processes, scanty febrile urine, frequent chills, leucocytosis, the frequent presence of septic organisms in the blood, early cardiac murmurs, rapid onset of the typhoid state, absence of thyroid fullness and tenderness, and exophthalmos.

The **psychoses,** as **melancholia,** acute **mania, dementia præcox** and the like, frequently enter into the symptomatology of a malignant type of Graves' disease and are discussed in the section on the Nervous System. Mention of **Paralysis agitans** and **chorea** is made in the same section.

Diabetes mellitus in Graves' disease is a topic which has been discussed very widely during the past several years. The frequency with which glycosuria occurs in hyperthyroidism, the hyperglycemia, the marked wasting of the body, polyuria, fatty stools and occasional hunger and thirst,—all these and many more phenomena occur in both conditions. It is no wonder then, that a diagnosis of diabetes mellitus is made when the above symptoms are prominent. Moreover, diabetes may actually coexist with exophthalmic goiter, gain the upper hand, and in rare instances, the patient may die of diabetic coma.

Geyelin states that the blood-sugar reading of 0.1 per cent or over should be considered a hyperglycemia. In moderate and severe types of this disease, it occurs in approximately 90 per cent of the case studies. In mild cases or during latent periods the percentage is commonly normal. In the absence of other pathologic conditions such as fever, alcoholism, asphyxia, neurasthenia, and the various endocrinopathies, the finding of a lowered tolerance to carbohydrates is of diagnostic significance in hyperthyroidism.

Dr. Paul Sainton (*Monthly Cyclopedia and Bulletin*), together with Dr. Paul Gastaud, has met with 3 instances of diabetes among 90 cases of exophthalmic goiter, and after an extensive search in literature has found altogether 60 cases presenting this combination of conditions. They estimate the frequency of diabetes in exophthalmic goiter as 3 in 100 cases. It is undoubtedly a fact that diabetes occurs much oftener in cases of hyperthyroidism than among patients with hypothyroidism, in which it is quite rare as Parisot has shown.

Commenting upon this subject, *The Medical Review* of August, 1914, says: "Clinically, diabetes occurring in the course of Graves' disease is manifested in two ways, viz.: (1) as a temporary or slight glycosuria, with the usual symptoms of diabetes only present in a trifling degree; (2) as a well-established condition, with all the characteristic symptoms present, the latter frequently even dominating the clinical picture as a whole. In the first group of cases slight thirst, or a slight increase in appetite, or a feeling of weakness is at times responsible for the examination of the urine which leads to the discovery of the glycosuria. The amount of sugar may be small, *e.g.*, 3.4 to 5 gm. in one of the author's cases with a total daily urinary output of 1,500 c.c. In the second class of cases, on the other hand, the diabetic disorder is usually severe, 8 to 14 liters being sometimes excreted daily, and the amount of sugar eliminated ranging from 340 to 1,000 gm. a day, or even attaining higher figures, such as are hardly met with in any cases other than those of pituitary diabetes. Polyphagia, polydipsia, and other symptoms are pronounced. It seems to be a uniform rule that in severe cases of Basedow's disease severe diabetes exists, while in mild Basedow cases slight and evanescent glycosuria occurs. In most cases diabetes appears as an epiphenomenon in the course of exophthalmic goiter, and a long time after its onset. Where both conditions have become established, a state of equilibrium seems to occur between them, viz.: when the Basedow condition becomes worse the diabetes improves, and *vice versa*. The prognosis varies in different cases. Mild diabetes in Basedow cases runs a course quite like that of arthritic diabetes, presenting the same intermissions and low degree of intensity. In severe forms, on the other hand, the combination of the two diseases constitutes a condition of exceptional gravity. In the series of cases collected by Sattler, 25 patients rapidly succumbed—7 of them in coma. Sometimes, as in one of the author's own observations, pulmonary tuberculosis is superadded, further aggravating the prognosis and hastening death.

"On the whole, the association of Basedow's disease and diabetes can not be considered a fortuitous phenomenon. That a bond of some kind unites the two conditions can readily be shown. Their mutual relationship is brought to light when one sees exophthalmic goiter and diabetes alternate in different members of the same family. Manby has reported 3 striking instances of this. In one family, the father and brother of a Basedow patient are diabetic; in a second, the sister of a Basedow patient is diabetic, and her brother's two children have been carried off by acute diabetes. In the third instance, the two sisters of a Basedow patient succumbed to a diabetes at the ages of nine and ten respectively. In a case of Pibrane and in one of the author's, the father of the Basedow patient was diabetic. Finally, in still another case the patient's aunt had diabetes and her cousin exophthalmic goiter. The inverse relationship in the severity of the two disorders in the same individual already referred to, is evidence in favor of their mutual dependence.''

For diagnostic purposes in general it may be stated that the absence in true diabetes mellitus of thyroid fullness, tachycardia, exophthalmos, tremor, moist clammy skin and rise of temperature, and, on the other hand, the absence in hyperthyroidism of *persistent* large quantities of sugar in the urine, very great output of urine, great hunger and thirst, itching, dry skin, and visual disturbances, will assist in differentiating the two conditions.

Hypothyroidism presents a syndrome just the reverse from that of hyperthyroidism. Since in some instances the two conditions seem in variable degree to appear in the same patient alternately or concomitantly, and since a state of myxedema may follow a state of Graves' disease, it will not be superfluous to append the following tabulation:

Hyperthyroidism	*Hypothyroidism*
1. Usually an enlargement of the thyroid.	Usually no enlargement of the thyroid, unless symptoms are secondary to a goitrous condition.
2. Alert expression, facies indicating a degree of perpetual anxiety or fright.	Expression is blank, stupid and bloated.
3. Insomnia.	Somnolence.
4. Increased nervous excitability; flow of thought and speech accelerated.	Diminished nervous excitability; flow of thought and speech sluggish.
5. Marked progressive emaciation.	Gradual increase in weight.
6. Skin moist and soft, dermographia; no mucinous infiltration of subcutaneous tissues.	Skin dry, harsh, puffy, scaly, mucinous infiltration of subcutaneous tissues.
7. Hair not much altered.	Hair becomes thick, brittle and sparse.
8. Temperature somewhat above normal.	Temperature somewhat below normal.
9. Often glycosuria and polyuria.	No glycosuria or polyuria.
10. Tachycardia and vascular throbbing.	Pulse slower than normal, often bradycardia; no vascular throbbing.
11. Exophthalmos and the various eye signs (Von Graefe's, Stellwag's, Moebius', Dalrymple's, etc.)	No exophthalmos or diagnostic eye signs. Eyelids puffy.

Hyperthyroidism	*Hypothyroidism*
12. Increased respiratory rate with diminished expansion.	No increased respiratory rate; often diminished.
13. Tremor of outstretched fingers, toes, and often of whole body.	No tremors.
14. Gastrointestinal functions hyper-active; appetite normal or increased; symptoms of nervous indigestion and diarrhea may occur.	Gastrointestinal activity sluggish; poor appetite and digestion, constipation.
15. Symptoms aggravated by thyroid extract.	Symptoms improved by thyroid extract.

CHAPTER VII

SHELL SHOCK (?) IN SOLDIERS*

That "shell shock" is a misnomer, and the term misleading in its implications, is the growing belief of most observers who have had the opportunity of carefully studying the syndrome of symptoms in the various base hospitals of Europe and America. The fact that many of these cases develop goiter and exophthalmos soon after the inception of the affection diagnosed as "shell shock" has cleared the path for a more thorough investigation of the etiology, physiology and symptomatology of this disease, as a result of which there is a growing conclusion that most cases of "shell shock" present symptoms in common with exophthalmic goiter, and in all probability the vast majority of these patients are subjects of either an aberrant or a true form of Graves' disease.

Goiter, associated with cardiac and nervous manifestations, has been a problem in armies of the past, but lack of clinical precision precluded any accuracy of description worthy of note. In the siege of Paris (1871) Graves' disease was common. In 1874, goiter was stated by Michaud to have been epidemic in the French army, and Corvisart described the effects of emotion upon the heart during the French Revolution. During the Civil War the symptoms of "soldier's irritable heart" were described by J. M. DaCosta; the chief manifestations were pallor, extreme weakness often to the point of exhaustion, paroxysmal dyspnea, tachycardia to 120 and over, often accompanied by arrhythmia and increased by physical and mental excitation, and prolonged diarrhea which was considered an etiologic factor. The group of phenomena formed an important part of a condition which occurred in many people who not only had been shocked by shell fire, but who, by their nervous makeup, feared to face it. Many instances occurred in civilians in regions where fighting had taken place or where fighting was imminent.

---

*This chapter, slightly modified, appeared as an article in the New York Medical Journal, July 5, 1919.

Sajous suggests that the excessive exertion incident to warfare with the excitement, rage, and fear, leads to functional exhaustion of the adrenals, resulting in loss of tone of the vascular system, exciting thyroid hyperactivity. He thus implies that this adrenal disturbance instigates a general endocrine instability leading to the Basedowian syndrome.

Alexander notes a case of Graves' disease following a bomb explosion.

Etienne and Richard, in a recent paper, relate that the repeated violent bombardments of Nancy from the big guns and aeroplanes resulted in a wave of cases of exophthalmic goiter among the civilian population, which were characterized by high blood pressure in some, glycosuria in others, and in some women arrested menstruation. In a man of thirty-six symptoms of Addison's disease appeared, and these were followed by symptoms of exophthalmic goiter. The hyperthyroidism subsided in three months, but the Addison's symptoms persisted to a fatal termination within eighteen months from the onset of the condition in two other cases. Addison's disease became superimposed on preexisting exophthalmic goiter. It is thus seen, as Sajous has often mentioned, that exophthalmic goiter of emotional origin may thus develop under the influence of a disturbed function of the suprarenal glands; on the other hand, suprarenal disease may also become superimposed on exophthalmic goiter, giving rise to bronzing of the skin.

The magnitude of the question of functional conditions in the World War, especially those classified as "hysteria," "shell shock," "irritable heart of soldiers," "war tachycardia," "neurocirculatory asthenia," "soldier's psychosis" and the like, is thus described by Colonel Pearce Baily: "The neurologic problem of war has assumed an importance quite undreamed of, and the necessity of neurologists for a modern army is receiving general recognition. In battle areas the need of neuropsychiatry exceeds that of general medicine, as the nervous and mental casualties may exceed 10 per cent of the total casualties. France maintains 20,000 neurologic beds in the rear, most of which are occupied by functional cases, and at the front tries to maintain one and one-half neurologic beds for each thousand troops. Major Arthur Hurst, R. A. M. C., estimates that 26,000 beds are occupied each year in Great Britain by purely hysterical patients.''

If we take into account the fact that Graves' disease is a chronic condition of ''fright, fight, and flight,'' as evidenced by the typical picture of perpetual terror in the well-developed case (bulging eyes, anxious expression, trembling of the body, etc.), we can readily reconcile cause and effect in our conclusion that war conditions are etiologic conditions through the production of a state of nervous or emotional tension which, no matter what term may be applied to the disease of the victim, is but a state of disturbed functional harmony between the ductless glands, during which there is especially a hyperactivity of the thyroid gland. In brief, we are in these instances dealing with one or the other typical or atypical forms of what is known in civil life as Graves' disease, Basedow's disease, Parry's disease, exophthalmic goiter, hyperthyroidism, or dysthyroidism. There is such a thing as mere irritability of the heart's action with slight increase in its rate, insomnia, and nervousness, which, though presenting little other evidences of Graves' disease must be looked upon as a ''larval'' or incipient form of the same, which may merge into a typical exophthalmic goiter on the persistence of the etiologic factors and the postponement of the proper remedial measures.

Dr. F. D. Smith, in reporting 116 cases of toxic goiter discovered among 65,507 men examined at Jefferson Barracks, concludes that the physical and mental strain of army life accentuates and renders more prominent a hitherto quiescent, incipient case of Graves' disease occurring in civil life, and suggests that toxic goiter is a poor military risk.

Dr. Harlow Brooks, in his study of the disturbed thyroid function in recruits at the Camp Upton Base hospital, states that he is surprised to find so many cases of hyperthyroidism among men. He concludes in his examination of cases in his official capacity, that the neuroses described under "shell shock," "irritable heart," and other allied terms, are due to hyperthyroidism which may be in many instances incited by infection or an unknown agent. That the prevailing cause is the environmental and the emotional tension, is suggested by the fact that those races of strong emotional element are most prone to this affection;—the Hebrews lead, the Italians are next, then come the Irish, and last of all the negroes. Tachycardia is the most striking symptom in nearly every instance, and this, plus palpitation, causes the recruit to apply to the doctor for treatment, exemption, or discharge. There is rarely an accompanying arrhythmia; the pulse rate is increased by physical or mental excitation; there is a marked throbbing of the superficial vessels, especially the carotids, brachials, and femorals, while the aorta in emaciated individuals could also be seen to throb. Brooks suggests that absolute differentiation of this condition from aortic insufficiency could be made by the graphic method of polygrams. The heart sounds, because of their rapidity, were usually difficult to analyze, but often a soft, systolic murmur was present at the apex, transmitted at times into the axilla. These murmurs seem to be functional and not organic in nature. Precordial distress is extreme in many cases and often radiates to the left shoulder. Vasomotor instability is evidenced by an alternating flushing and paling of the face, dermographia, low blood pressure, and capillary pulse. Vertigo, syncope, and outbursts of emotionalism are often precipitated by a sudden call for an examination by the physician. Occasionally such nervous phenomena as epileptiform attacks, convulsive spasms, crying, outbursts of temper, and moments of extreme terror are manifest. Most of the time these patients appear very weak, but attempts at sleep are futile as the insomnia is complete. Tremor is almost constant, occurring in the outstretched fingers and toes, and ofttimes through the whole body, just as in civilian life a rise in the afternoon or evening temperature, marked sweating, especially at night and dyspnea on the slightest exertion are very characteristic. In Brooks' cases, two-thirds of the patients presented a definite thyroid hypertrophy, in some cases amounting to actual goiters, the individuals complaining of a choking sensation, though they but rarely described a globus hystericus. A considerable number of Brooks' cases gave an ancestral history of goiter, particularly on the maternal side, and in many instances, a family tendency to nervous instability, hysteria, insanity, perversions, or genius. Exophthalmos was also present in longstanding cases, sometimes developing suddenly. Those patients endured the acute infections very badly; tobacco produced in them much more serious symptoms than the average, and they had a distaste for alcohol. It may be remarked that the tachycardia was not altered by digitalis, even in massive doses. The nitrites markedly increased the symptoms, and there was a general hypersensibility to the vasomotor dilators. The diagnosis of hyperthyroidism was confirmed by the adrenalin test.

J. Barr is also of the opinion that the thyroid is largely at fault in "soldier's heart" or "shell shock." He believes that the influence of the gland is primarily exerted upon the calcium metabolism which in turn affects the action of the heart. The condition first appearing is likely to be hyperthyroidism followed by hypothyroidism.

Wilson, Poynton, and Stoney, in a symposium, refer to the possible thyroid etiology of "soldier's heart." Wilson observed thyroid enlargement in about one-ninth of his cases; thyroid medication seemed to augment the symptoms. Poynton and Stoney suggest the use of x-ray treatment of the thyroid in cases of undoubted thyroid involvements.

P. Hernaman-Johnson and P. C. White state that soldiers from the front who suffer from so-called irritable heart are found to have been subjected to great strain. The symptoms which they find most prominent are palpitation, slightly elevated temperature, enlarged thyroid, rapid pulse, dyspnea, tremor, insomnia, irritability and emaciation. These authors emphasize their belief that the condition commonly called irritable heart is really a form of Graves' disease.

F. A. Stoney, in discussing the connection between "soldier's heart" and hyperthyroidism, emphasizes the likelihood of confounding mild goiters following "shell shock" with neurasthenia and the symptomatology of incipient exophthalmic goiter. The onset of the illness usually dates back to some severe shock as that produced by a bursting shell or a burial. These soldiers are sent back to base hospitals with such diagnosis as "shell shock," "neurasthenia," "early phthisis," and "soldier's heart." Examination of these hearts proves them to be typical of early Basedow's disease and are characterized by practically normal rate when lying down and increased rate, 90 to 100 per minute, when standing or sitting. Not infrequently the heart is dilated, the action tumultuous and irregular in force and rhythm. The characteristic sign on auscultation is a brief first sound lacking in tone; murmurs are often present. In addition, there are such subjective symptoms as fainting, weakness, dyspnea, giddiness, precordial pain and palpitation, all of which characterize Graves' disease. The diagnosis is confirmed by such findings as perspiration, tremor, nervousness, and the other typical signs and symptoms.

Rothacker cites three cases from military life, which showed an acutely developing Basedow's disease caused by the nerve concussion, the excitement of machine-gun fire and trench warfare. After a rest of several months all three made an uneventful recovery. Many similar cases were seen by Rothacker. These were often at first considered as heart disease, but a close study of their histories revealed typical acute Basedow's disease. These subjects were unfit for field service in modern warfare, as the exhausting long marches in water-soaked districts, the continuous fighting, and the forced marches by night and day caused overacting hearts, slight rises of blood pressure and nervousness.

K. W. Ney incorporates in a report on military surgery the fact that a large number of cases sent to the European base hospitals from the firing line come there with a diagnosis of general fatigue and tachycardia. These patients are sent in by the hundred, and in many cases absolute rest in bed and digitalis fail to cause abatement of the symptoms. These patients can stand no exertion, and even while at rest the heart action is very rapid. Many of these subjects remain in the hospital for months, during which time they develop a gradual enlargement of the thyroid gland. These cases, Ney believes, indicate a derangement of the ductless glands, especially the thyroid, through a disturbance of the emotional balance.

C. Boir of Berlin describes three cases in which soldiers, after a great fright, showed a classical picture of Graves' disease.

Moon, Roussel, and the writer have observed that a frequent predisposing cause in the production of conditions simulating hyperthyroidism in the recruit is nicotine poisoning. The various movements throughout the country for the purpose of sending large quantities of cigarettes to our boys "over there" may have had their merits. Confirmed smokers have probably been benefited by an ample supply of the weed, for it must be admitted that its loss would have wreaked havoc with their nervous systems. On the other hand, many young men who have never smoked at all or have smoked but little, have had forced upon them the idea that continuous smoking is the boon to a feeling of well-being, and it is among this class especially that thousands of cases of invalidism occurred through a greater predisposition to neurocirculatory diseases.

From a careful examination of the conclusions and deductions of the various observers herein mentioned, and many others, it is obvious that we must classify differently these conditions heretofore noted as "shell shock," "irritable heart of soldiers," "neurocirculatory asthenia," "early phthisis," and the various other terms employed as a cloak for lack of clinical precision. It seems clear that, in view of the fact that a large percentage of cases, perhaps the majority of them, present evidences of thyroid hyperfunction, the totality of cases herein discussed must of necessity be divided into two classes: (*a*) those cases which are probably not due to hyperthyroidism (the minority), and (*b*) those cases which are manifestly due to a hyperactive thyroid, *i.e.*, Graves' disease (the majority).

(*a*) This class which can not be placed in the category of hyperthyroidism probably requires further and more minute subdivision, if one is to employ accurate terminology. These patients have probably some inherited tendency toward the various forms of neurotic disturbances. A careful investigation of the family history usually reveals the fact that there is a trend toward epilepsy, migraine, melancholia, dementia, neurasthenia, hysteria, or one of the forms of insanity, on the maternal, paternal side, or both. This acting as a predisposing factor, all that is necessary to disturb the balance of the higher cerebral centers and its related forces is the exciting causes of warfare. Mere passive observation of casualties such as the picture of wounded being brought in on stretchers is often sufficient to destroy the balance of an individual who was formerly characterized as normal. How much more liable is this predisposed creature to neurasthenia, hysteria, melancholia, or even dementia or mania, when he is in the presence of actual fighting with bombs exploding about him and his comrades falling before his very eyes, often reduced to unrecognizable masses of flesh! A person whose mental inheritance is irreproachable quickly extricates himself from this psychic difficulty, and in the heat of the strife, reconciles himself to the great moral principle involved and fights on to victory. But the creature in question, whose mental balance has wavered, is as badly off as one whose physique has been paralyzed by a shell. He becomes a useless entity, if not an impediment to the favorable progress of the moment's events and must be quickly removed from the scene. These patients, as a rule, are subjects who are finally classified as cases of melancholia, neurasthenia, hysteria, hysteroneurasthenia, acute mania, dementia precox, and the like, and must be treated as such in much the same fashion as cases occurring in civil life.

(*b*) With respect to this class, probably the great majority of cases, it is concluded by nearly all physicians that emotional shock is the greatest exciting factor in the instigation of the Basedowian syndrome. If this be true, what situation presents a greater degree of emotional shock than the condition of actual warfare in which the sense of self-preservation is so keenly involved? The question of predisposition is still moot. It is thought by many that here also there must be some predisposing inherited tendency toward the disease, for why should ninety-nine out of a hundred men in a given situation remain normal while one man becomes a victim of Graves' disease? It certainly seems as though the afflicted one must have a special susceptibility. But this question is still open.

The diagnosis of incipient hyperthyroidism is often fraught with difficulty. The diagnosis of "irritable heart of soldiers," "shell shock," "early phthisis," and the like, are not without cause, though erroneous, but are based upon observed phenomena which are just as misleading in civil as in military practice. The elusiveness of the early stages of the thyroid hyperfunction has led many otherwise able diagnosticians to deductions totally at variance with existing factors, which latter soon proved to be a state of endocrine instability. The main reason for this difficulty lies in the fact that the most important signs of exophthalmic goiter, *i.e.,* exophthalmos and goiter, are usually late in coming, and in their absence diagnostic pitfalls are met with. As a rule the earliest manifestation of hyperthyroidism is the tachycardia associated with subjective precordial symptoms; this in combination with the nervousness, insomnia, and anorexia, easily leads to a conclusion that the subject is suffering from "irritable heart," which, by the way, is an unscientific diagnosis, merely indicating a symptom. The differentiation between this and the tachycardia of incipient hyperthyroidism is easily made; a rapid heart not due to a surplus of thyroid substance in the blood is usually capable of being slowed by digitalis and by sleep. In the tachycardia of hyperthyroidism, digitalis and sleep have little if any effect upon the rapidity of the heart's cycles. The diagnosis of "shell shock" is again just as misleading as the term "ediopathic" when placed before the term epilepsy, or the term "essential" preceding the terms anemia or asthma. They are mere words and tell us nothing, serving as a cloak for our ignorance. Under "shell shock" were included until recently nearly all patients who were not suffering from actual physical injury; but the gradual assertion or injection into the clinical picture of certain other signs and symptoms in these instances led to a more careful and scientific classification in course of time. "Early phthisis" is frequently the diagnosis based upon the rapid emaciation, deficient respiratory expansion, a slight rise in afternoon temperature, and excessive sweating, all of which are present in hyperthyroidism, and it is indeed often difficult to distinguish between the two. Occasionally one meets with a case where hyperthyroidism and phthisis occur in the same patient, and here the difficulty of diagnosis is great indeed; but under ordinary circumstances, the absence of cough and expectoration and of a daily chill, the absence of definite pulmonary lesions and the presence of the peculiar physiognomy (even in the absence of exophthalmos), the persistent, marked tachycardia, and the slight fullness of the thyroid gland especially when the head is thrown backward,—all these serve to solve the problem. Occasionally certain laboratory tests are made to confirm our deductions, among which may be mentioned an x-ray examination of the chest, the tuberculin test, and the Goetsch adrenalin test. Careful examination, then, and laboratory observation, should rarely, if ever, fail us in the proper diagnosis when hyperthyroidism is a possibility.

Having classified a given case as one of hyperthyroidism or dysthyroidism (a better term to employ), what is to be done to restore the individual to former stability of body and mind? How are we to place this man back again into his civil environments as a useful citizen of the community and a wage earner, with the possession of his normal standard of health and life expectancy? This question resolves itself into one respecting the mode of therapeusis to employ. This is easily answered: Treat the patient as carefully as you would a case of exophthalmic goiter in civil life,—nonsurgically, as herein outlined.

CHAPTER VIII

DIAGNOSTIC TESTS IN EXOPHTHALMIC GOITER

In addition to the signs and symptoms herein enumerated and which are in themselves sufficient to serve us in the diagnosis of the majority of cases of Graves' disease, the following tests, though not of absolute importance, have been found of service in instances of doubt and also for the purpose of confirming our convictions:

The Goetsch Test.—This test is both a local and systemic reaction to adrenalin in the presence of a surplus of thyroid hormone in the blood. Eight minims of a 1:1,000 solution of epinephrin are diluted with an equal quantity of sterile water and injected hypodermically into the arm. In the presence of hyperthyroidism, there is immediately formed an area of blanching around the point of injection, and about the margin of this, usually a red areola gradually shading off into the surrounding tissue. In about half an hour the center of the white area becomes bluish gray to lavender, and at the end of about one and a half to two hours the red areola takes on the bluish or lavender color, while that in the center disappears. This lavender areola remains for about four hours from the time of injection and is the most characteristic part of the test. The reaction in a normal person lasts from thirty to forty-five minutes, but in one suffering with thyroid toxemia (either primary or secondary) the phenomenon lasts from one and a half to two and one quarter hours. Accompanying the local reaction may be an increase in pulse rate with palpitation of the heart and an exaggeration of the tremor and nervous symptoms in general. The heart rate is increased from 10 to 50 above its former rate. In half an hour there is a moderate fall followed by a secondary rise and fall, the normal point being reached in about ninety minutes. In addition, there is a variable increase in the tremor, asthenia, throbbing, and apprehension. Vasomotor changes, such as a sudden pallor of the face, lips, and fingers, due to vasoconstriction, are followed within thirty minutes by a stage of vasodilation with flushing of the skin and sweating. A slight rise in temperature and polyuria are also observed.

In commenting upon this test, an editorial in "Endocrinology" (Volume II) states that in order to interpret a test as positive it is regarded as necessary to have a majority of these signs and symptoms definitely brought out or increased. Thus there is at times a considerable increase of pulse rate without much increase in systolic blood pressure, but with a considerable increase or exacerbation of the objective signs and symptoms; or there may be an increase of ten points in the pulse and blood pressure and a moderate increase of the symptoms and signs; or again, there may be only slight changes in pulse and blood pressure and considerable change in signs and symptoms. These may be regarded as positive. In a word, then, one must consider the entire clinical picture produced in order to gain a correct interpretation, just as in the disease itself one can not expect every one of the characteristic signs and symptoms to be present in order to make a diagnosis. A considerable degree of correspondence between the severity of the disease, clinically, and the reaction has been noted.

This test is valuable in borderline cases,—instances which do not present clearly or at all a sufficient number of earmarks characteristic of the Basedowian syndrome. Thus the mild *fruste* forms and cases primarily diagnosed as neurasthenia, hysteria, and even one of the insanities may be discovered to be merely aberrant forms of hyperthyroidism.

The Pituitary Test.—Originated by Bondouin and Porak (quoted by McCarrison), this test is also employed to detect an excess of thyroid secretion in the blood. One c.c. of an extract of posterior lobe of the pituitary body injected into the patient causes slowing of the pulse within two minutes which in Graves' disease passes off in seven or eight minutes. In normal persons the pulse is accelerated by this injection, attains its maximum in five or six minutes, and returns to normal within fifteen minutes.

Basal Metabolism.—Dr. George W. McCaskey, of Fort Wayne, Ind., is in accord with Means and Aub in believing that the basal metabolism bears a relation to the neuromuscular and those phenomena relating to the respiration, circulation and secretion. A hyperstate corresponds to increased metabolism and a hypo- to decreased metabolic rate. McCaskey emphasizes the fact that metabolism corresponds to heat consumption or oxygen consumption, and states that Benedict's apparatus measures this rate by the number of calories per square meter of body surface per hour. A 10 to 20 per cent increase in consumption is indicative of a mild case; 20 to 50 per cent, a moderate case, 60 to 70 per cent, severe, and 70 to 100 per cent very severe. As these cases are not constant in the metabolic rate, the reading is reliable only for the time that the observation is made, but it is also of value in studying the *course* of the disease.

The Hyperglycemia Test.—McCaskey states that this test is of confirmative value. 100 gm. of glucose fed to a normal person does not produce hyperglycemia in one hour. McCaskey claims that every reading of over 1-10 of one per cent represents a hyperglycemia when tested with a fasting stomach. Even in borderline cases a marked hyperglycemia is noted. He is of the opinion that an increase in basal metabolism and a hyperglycemia, while not actually pathognomonic, are of valuable corroborative evidence in thyrotoxicosis. He does not place absolute reliance on these tests as indicative of thyroid hyperactivity *per se*, but as corroborative of hyperthyroidism as a concomitant feature of a general endocrine disturbance.

N. W. Janney states that hyperglycemia seems to be indicative of hyperthyroidism, but glycosuria is of no special pathognomonic value. He believes that more accurate work is needed on the technic of these tests, and that they should be applied chiefly to borderline cases, where they are most needed. Janney states that results similar to those obtained in hyperthyroidism are procurable in cases of pituitary and adrenal disease, and that the apparatus of Benedict is by no means as simple as it appears to be.

It must be concluded that, valuable as these basal metabolism and hyperglycemia tests may be, their importance is but relative, and the deductions drawn are interesting only in that they form the first stage of a series of clinical experiments along these lines of endeavor.

The Thyroid Extract Test.—This test is not delicate, but is interesting and useful. The administration of thyroid extract in subjects of hyperthyroidism markedly accentuates the symptoms although, strange to say, improvement may occur in isolated instances.

Harrower recommends four daily doses of ½ grain, 1 grain, and 2 grains of U. S. P. desiccated thyroids respectively. Ordinarily, three days suffice for the test, though it may be advisable to continue the pulse record for one or two days before, and two or three days after discontinuing the capsules. Harrower gives his patients the following written instructions:

"Take one small capsule at eight, ten, twelve and two o'clock. Make a note of the pulse rate, after resting at least ten minutes, at nine, twelve, three, six and nine p. m. On the second day repeat this procedure, using the medium-size capsules, and on the third day use the large capsules in the same way. Do not eat or drink within half an hour of counting the pulse. It is best to arrange to eat after counting, as a full stomach sometimes modifies the rate. Always maintain the same position, preferably sitting, when counting. It is essential that hurry and exercise immediately before counting be studiously avoided. Keep a record of the pulse variations for a day and a half after the capsules are taken, or for five days in all. Carefully enter the findings on the chart. Note any other manifestations which you think may be connected with taking the capsules on the back of the chart."

The *blood* examination is considered one of diagnostic and prognostic significance by some observers. The leucopenia, at the expense of the neutrophile polynuclear leucocytes, and the relative increase of lymphocytes, combined with Stellwag's sign and tenderness over the enlarged thyroid are considered by Kocher as conclusive of the diagnosis of Graves' disease. The blood findings in other thyroid affections are practically similar to the above, rendering this test of relative value only.

The Digitalis Test.—With respect to the tachycardia, this test is of value. The heart-hurry of exophthalmic goiter is constant, day and night, and is not slowed by digitalis, even if given in large doses.

Certain *complement-fixation* tests have been attempted and described by clinicians interested in endocrinology, but they are still in the experimental stage and unreliable.

CHAPTER IX

COURSE AND PROGNOSIS OF EXOPHTHALMIC GOITER*

Recovery from any disease means restoration in the patient of the normal tissue metabolism, the return of the proper equilibrium between internal relations and external circumstances, the resumption of the proper function of all the tissues and organs of the body, the harmonization of each organ and function with all the other organs and functions in the great chain of events constituting normal animal life. A person can not be said to have recovered from a disease until he is at perfect ease, restored to the normal state of thinking, acting, and feeling, with the possession of his maximum standard of happiness and his maximum standard of usefulness to self and society.

As we are here concerned with a morbid process in which there is a surplus of thyroid substance in the blood, we ask ourselves: What are the factors capable of influencing the course and prognosis of the disease? or more directly: What are the stipulations respecting recovery from this condition most commonly known as exophthalmic goiter?

Generally speaking, the subject of exophthalmic goiter may be considered cured when the active process of thyroid intoxication has been made to cease. In other words, the patient is considered on the way to cure when the saturation of the blood with thyroid substance is no more a factor to be concerned about, and when in all likelihood, at least for the immediate future, this etiologic exciting cause (or causes) of the Basedowian syndrome is no longer existent. Having secured a cessation of the hyperactivity of the thyroid secretion, the next step is the repair of whatever damage there has been wrought in the patient's organs and functions during the entire course of the disease.

---

*This chapter, slightly modified, appeared as an article in Archives of Diagnosis January, 1919.

It is well to remember that no matter how mild a disease appears, there is always a certain amount of permanent damage to this or that part of the economy, just as there is always a variable degree of scar tissue remaining after a laceration of one of the tissues. This is more likely to be the case in a disease like exophthalmic goiter in which nearly every tissue of the body (especially that of the nervous and circulatory systems) is in the hyperactive state, and it can not be hoped, even in the most complete recovery from this disease, in view of the marked degenerative changes occurring in the cellular structure, that they could become entirely well again from a *histologic* viewpoint. So that the word cure, even at its very best, is but a relative term and concerns more the patient's subjective feeling, his practical usefulness and relative longevity rather than the complete pathologic or histologic restoration of each individual cell concerned in the morbid process.

Mortality of Graves' Disease

Hector Mackenzie states that during the four years, 1911-1914, the number of deaths returned in England and Wales as resulting from exophthalmic goiter was 1,558 for females and 155 for males, a proportion of ten females to one male. The number of deaths increase in each five-year-age-period up to 35-40. The author states that the disease is very rare in childhood, that he has yet to see a typical case under the age of twelve. In 3 of the fatal cases the duration of the disease was less than six months; in 10 less than one year; in 12 less than two years; in 8, less than six years; and in 6, over six years. In more than half of the cases it was less than eighteen months.

McCarrison claims that in a large number of cases collected for statistical purposes "death occurred in 11.8 per cent of cases from Graves' disease itself, death usually occurring from six months to six years after the onset of the malady; in over 50 per cent of cases it occurred within 18 months." The question arises, what is meant by "death from Graves' disease itself?" If he means death from exhaustion through the persistence of the cachexia as a consequence of the hyperthyroidization of the vital functions and especially of the metabolic changes, these figures seem highly plausible and may be considered as fatal terminations *directly* due to this disease. But we have to account for death *indirectly* due to Graves' disease which must also be included in this mortality, and if this be acceptable, then the mortality of Graves' disease rises considerably, perhaps to 18 or 20 per cent.

In addition to the fatalities from "Graves' disease itself," as stated, what are the indirect causes of death during the course of hyperthyroidism?

1. Heart failure or loss of compensation due to the profound degeneration from the overactivity of the myocardium. This condition is quite common, as it is not unusual to see a patient with advanced Graves' disease who possesses all the evidences of failing compensation, i. e., mitral and tricuspid regurgitation, cyanosis, dyspnea, and beginning anasarca. These cases are usually as hopeless as those of primary progressive endocarditis.

2. Tuberculosis frequently either coexists at the onset of the Basedowian syndrome or asserts itself some time during its course. A patient of this class, though possibly possessing a latent focus somewhere in the economy might never have known of his affliction were it not for the fact that the hyperthyroidization has so lowered his bodily resistance that the focus in question has now flared up and is becoming a factor which promises to be of dominant importance, threatening his very existence.

3. Insanity in some form, complicating Graves' disease, may so exhaust the patient through outbursts of marked excitation as to lead to a fatal termination far before the Graves' disease itself has advanced to any degree of peril.

A very grave omen is mania, as it forebodes imminent death.

4. Myxedema may be superimposed upon or succeed a typical picture of hyperthyroidism and thus precipitate a fatal termination through hypothyroidism. The gradual occurrence of the hypothyroid changes may give rise to a false sense of security because of the gradual disappearance of the symptoms of Graves' disease. The heart becomes slowed, the exophthalmos improves, the nervous manifestations become less marked, sleep is better, the patient gains in weight, and the skin is no longer moist. But sooner or later the patient begins to feel bulky, there is persistent somnolence, the skin, especially of the face, becomes puffy, dry and of waxy hue, the features expressionless, there is mental torpidity; constipation and tympanites replace the former diarrhea, and general physical and mental deterioration is progressive. Thus, instead of spontaneous cure, as we thought had occurred, we are confronted with a typical case of myxedema. Granger (quoted by McCarrison) states that the cycle from thyroid hyperplasia to fibrosis and thyroid deficiency occupies, on the average, about six years.

5. Cachexia strumipriva, resulting from the removal of the entire thyroid gland, usually leads to death within five years.

6. Tetany, due to the removal of the parathyroid glands, a not uncommon accident even in the hands of expert surgeons, may quickly prove fatal.

7. Diabetes mellitus may in rare instances precede, intercur, or follow some time after the onset of hyperthyroidism, sooner or later assuming ascendancy. For such a patient the diabetes itself might not have jeopardized life for a long time, had it not been for the extreme devitalizing influence of the coexisting hyperthyroidism.

8. Miscellaneous intercurrent affections,—nephritis, fatal syncope, pneumonia, influenza and the like, may lead to fatal termination. In this connection, it is interesting

to note that an operation on a patient suffering with Graves' disease adds 13 per cent to the recognized mortality rate of said operation, according to Barton C. Hirst. In other words, hysterectomy, which has a mortality rate of 3 or 4 per cent, would, in a patient suffering with exophthalmic goiter, entail a risk of 16 or 17 per cent.

As both physician and patient are more concerned with the question of cure than with that of mortality of the disease, we restate the question: What factors are capable of influencing the course and prognosis of the disease? The following are the most important, divided into intrinsic and extrinsic:

Intrinsic

Under this heading we include the following factors capable of influencing the course and prognosis of exophthalmic goiter, and which exist directly or indirectly within the patient:

1. Age and sex. The younger the patient, the more severe the symptoms; in this respect, the disease resembles in its course such affections as tuberculosis and diabetes mellitus. My youngest case was a girl of thirteen whose course promised to be rapidly fatal until abruptly checked by appropriate remedial measures, the case resulting in cure within about fourteen months. My oldest case was a physician of sixty-four, a professor in a prominent university, who had been suffering with hyperthyroidism for three years, and although there were moderate exophthalmos, marked thyroid fullness, a typical tremor and a heart-rate of 92, he appeared almost normal to the casual observer.

In the male, the symptoms are more apt to assume a rapid and fatal course than in the female. True cachexia, extreme weakness, tachycardia, emaciation, and a diarrhea, which is likely to result in profound depression, frequently characterize the male cases.

2. The previous condition of health of the patient, by virtue of the degree of the recuperative power of the organs

and structures of the body, would materially alter the course and prognosis of the disease. A frail, anemic, nervous woman would, of course, be far more seriously affected by hyperthyroidism than one who was formerly robust, stolid and plethoric. In this connection, it must be observed that, since Graves' disease is characterized essentially by an extreme hyperoxidization in the metabolic processes, with rapid loss in weight, a patient who was formerly overfed would not be as apt to become so weak and emaciated as one who had no weight to spare.

3. The digestive system, if markedly depraved, would impede satisfactory improvement in the patient. If the stomach is incapable of digesting a quantity of food not only sufficient to maintain the present weight of the patient, but to favor an increase in avoirdupois so that the subject may regain that which was lost, then the digestive functions require expert management, for upon them depends the fate of the case in hand. Typical symptoms of nervous indigestion with pain and discomfort after eating, nausea, pyrosis, and a continuous sense of fullness in the epigastric region, are commonly met with in subjects of exophthalmic goiter. Moreover, the intestines are frequently the seat of abnormal function in the form of distressing diarrhea or, less frequently, fecal retention with autointoxication. The latter has often an etiologic bearing upon the disease. The course and prognosis of the disease, then, will be materially affected by the presence or absence of gastrointestinal abnormalities. Generally speaking, a patient whose digestive functions keep pace with the ingestion of a quantity of food corresponding in caloric value to a gradual increase in weight and strength, is one whose course will be entirely favorable and will be restored to health within a reasonable time. Contrariwise, a patient whose digestive functions are rebellious and who in spite of expert therapeusis and dieting will show no progress, will have a very difficult uphill struggle which may suddenly assume a rapid downhill course.

4. The heart is of paramount importance in consideration of the prognosis in Graves' disease. Presupposing a heart previously normal in structure and function, a syndrome during which the organ is accelerated but to the extent of 80 or 90 cycles per minute may continue on indefinitely without marked damage to the myocardium; but a heart which beats away at 120, 140, and even 160 per minute is one which will rapidly give out through degeneration of the musculature with consequent hypertrophic dilatation, relative insufficiency, first of the left side of the heart, then of the right, and finally a fatal loss of compensation. Very frequently a beginning failure of compensation will be gradually but surely restored to health by the institution of proper remedial measures, and the heart, becoming slowed to a practically normal rate, will regenerate sufficiently to contract to within the normal limits, with a clinical cure. I recall such a patient with a marked mitral lesion from dilatation of the heart, in whom there was edema of the legs to above the knees and a considerable amount of ascitic fluid in the abdomen, completely cured in this way within a few months.

5. The nervous system with its intricate ramifications and manifestations is of prognostic importance. The insomnia, exhausting the patient from every possible viewpoint, the gastric and intestinal neurosis, interfering with the proper digestion and assimilation of food and engendering autointoxication, the bladder neurosis, a not infrequent symptom rendering the patient unable to retain a normal quantity of urine, with consequent nocturnal and diurnal frequency of micturition, the change in the patient's disposition, who is now morose, now melancholy, now hysterical, and occasionally merges off into a period of mania or dementia,—all these central and peripheral symptoms considerably alter the course of Graves' disease in any case, especially should the nervous system become the point of concentration of the Basedowian process.

6. The severity and duration of the disease, as in other morbid processes, would influence the prospects of recovery. The "acute" form of Graves' disease, fortunately but rarely met with, is rapidly fatal as a rule, no matter what the treatment. The symptoms are accentuated and markedly precipitous in occurrence, the course is brief and malignant in type, and the patient dies of exhaustion within from four to five or six weeks.

The course of the usual or "chronic" form of the disease is such that ample opportunity is offered the medical attendant for rapidly successful therapy if the diagnosis is made early enough. The earlier in the disease the proper measures are instituted, the more prompt are the results produced, for the vital organs are not yet sufficiently damaged in structure to affect the patient's welfare in later life, neither are they so habituated to morbid function as to render the restoration of a proper physiologic balance a tedious matter. In general, then, it may be remarked that a subject having suffered from this disease for from twelve to eighteen months, all things being equal, is fully capable of prompt recovery. A case of three or four years' duration offers many difficulties, though not at all incurable by appropriate therapeusis.

7. The presence or absence of complications is here, as in other diseases, a factor to be taken into account. In rare instances, the thyroid gland will undergo malignant changes, and a case of this sort soon becomes fatal. Occasionally, marked pressure symptoms upon the larynx, esophagus, or even the contents of the carotid sheath, by a goiter either anomalously situated or excessively large, will urge the necessity for surgical interference, with its mortality consideration. This latter complication is one occurring in the secondary or "Basedowified" goiter as a rule.

Tuberculosis, either preceding, coincidental with, or subsequent to the onset of Graves' disease may so further devitalize the patient as to render the prognosis much graver than otherwise. It might be suggested here that the most rapidly fatal cases of Graves' disease are probably of this sort.

Diabetes mellitus has been noted as a complicating disease. It is difficult in some of such instances to differentiate between genuine diabetes mellitus and the transitory glycosuria often seen in hyperthyroidism. Due caution must be taken in such cases, for, although on the one hand, antidiabetic treatment must be instituted, rendering the prognosis much graver through the restricted diet and greater starvation of the body, on the other hand, this procedure is unnecessary; and glycosuria may be practically ignored, the patient may be fed liberally, and the prognosis is much better.

Pregnancy may or may not be considered a complication during the course of exophthalmic goiter, but it certainly must receive attention. The marked demand made upon the body by the growing fetus must be compensated for by an ever-increasing quantity of ingested and assimilated food on the part of the patient, and where this is unsuccessful, we have two lives at stake. Moreover, when these cases do not abort spontaneously through the extreme irritability and hyperactivity of the nervous and other functions, there may be an accidental abortion through the administration of the various drugs, especially ergotin, or after thyroidectomy, if we do not observe due caution. Generally speaking, these cases do not progress well and have a very difficult struggle for health, at least until after abortion or the birth of the child at term, as the case may be.

8. The social condition of the patient will alter the course and prognosis of the disease in so far as the matter of proper quantity and quality of food, hygienic surroundings and conservation of energy are concerned. The patient amply supplied with this world's goods is fully capable of obtaining a proper supply not only of the most nourishing food, but the very best and freshest obtainable, as well as a proper variation consistent with a high degree of palatability. Such a patient will be favored with a prompter increase in weight

than one less favored with the necessary wherewithal. The essential hygienic surroundings,—proper care of the household, especially the chamber which the patient occupies, the matter of personal hygiene and its attendants, all these, if afforded, add to the grand total of beneficial progress. Furthermore, in a disease like exophthalmic goiter, where the heart and nervous systems are taxed to their utmost, the absence from vocation for a prolonged period, that is, a leisurely life for an indefinite time in the interest of the conservation of energy, is highly desirable and is the most effectual means of securing as nearly as possible a complete restoration to normal of the myocardial tissue.

The cooperation of relatives and friends is of importance, inasmuch as it bears directly on the mental poise of the patient. Inquiring friends, or those who possess a morbid curiosity tending to entice the patient into talking and thinking about her condition, are as a dose of poisonous medicine and invite relapse. The household should be cheerful, quiet, and characterized by an atmosphere of constant tranquility and harmony. Due caution must be given against shock or any kind of excitement which would tend to send the patient off into an outburst of emotion. A positive atmosphere, therefore, is one which favors the improvement of appetite, lessening the heart rate and the excitability of the nervous system, and enhancing recovery. A negative atmosphere, a household which excites, irritates, and otherwise perpetually disturbs the mental and physical equilibrium of the patient, produces the opposite effect.

9. Cooperation of the patient is highly desirable in the treatment of this disease, if we would hope for a favorable course and prognosis. The patient who promises to do everything and does little, will in course of time succeed in bringing about her end. There must be strict understanding with the patient that the regimen outlined by the doctor must be rigidly adhered to in letter as well as in spirit. The diet, bathing, rest, exercise, conversation, reading, time of retiring, sleep, hour of arising, all must be attended to

with enthusiasm and clocklike exactitude, if we would win the battle for health promptly and completely. Physician, nurse, relatives, and friends,—all must bear in mind that the slightest leeway or indulgence given the patient, in any way compromising the precision of the patient's regimen or transaction of the day will hinder an otherwise favorable progress and diminish the chances for recovery.

Extrinsic

Under this heading we include the following factors capable of influencing the course and prognosis of exophthalmic goiter, and which do not either directly or indirectly exist within the patient:

1. *Early diagnosis occupies first place in this category.* Exophthalmic goiter, at least in its incipiency, is the most elusive disease in the practice of medicine, since it simulates closely so many diseases commonly met with.

"If the average course of the disease be represented by a curve, the greatest height of the intoxication is found to be reached during the latter half of the first year and then rapidly drops to the twelfth month. In many instances it reaches the normal base line during the next six months, but more often it fluctuates with periods for the next two to four years. Secondary symptoms and exophthalmos may remain, but the active course rarely continues over four years without distinct intermissions. The ascent may be gradual, sudden, or irregularly marked by many secondary curves" (Plummer). Unfortunately, then, the clear-cut set of cardinal symptoms appears when the diseased process has already existed for some time and has made deleterious inroads in the form of cellular degeneration and devitalization into the circulatory and nervous systems. The four cardinal symptoms usually occur in the following order: there is a gradually oncoming feeling of weakness, especially in the calves of the legs, and a gradual loss of weight and strength; after a few weeks, the patient begins to experience precordial distress and palpitation, especially on physical or mental excitation. At this time, if the patient be a man, he will discover that the collars which he has been wearing are becoming too tight and will begin to suspect that there is a slight thickening over the front of the neck; soon the members of the family or friends will observe a change in disposition and a marked tendency, on the slightest provocation, to a disturbance of the usual mental poise; by and by the patient or friends will begin to observe a peculiar stare in the expression not unlike a degree of fright or terror, which soon manifests itself as a distinct bulging of the eyes; and in the course of time, or possibly during the incidence of the foregoing manifestations and hitherto unobserved, the tremor of the outstretched fingers will be noticed. The blending of one cardinal symptom into the other or their superimposition may require weeks or months, but there is a certain duration of time necessary to have them all noticeable concomitantly as a *typical* picture of exophthalmic goiter. It is the transitional stage between the first symptoms and the occurrence of all the rest that is the period of doubt, so to speak, and offers many pitfalls to the general practitioner in the diagnosis of the case.

Accordingly, then, an early diagnosis and early treatment offer much brighter prospects for prompt and complete cure than a belated diagnosis and the institution of treatment after certain changes in the various organs and tissues of the body have been incurred.

2. *Shall treatment be surgical or nonsurgical?*—Presented with a case of exophthalmic goiter, the first question which arises is: Shall we operate or not? We can only answer this question by the results which thyroidectomy seems to offer at the various clinics and hospitals, and also the results obtained by careful internists in the nonoperative treatment of the disease.

Stanton, in a study based on the analysis of some 1,600 cases found in literature, arrives at these conclusions:

"Removal of a portion of the thyroid gland of patients suffering with exophthalmic goiter produces a profound immediate effect noticeable within a few days of the operation and characterized chiefly by an improvement in the subjective symptoms of discomfort felt by the patient, but also accompanied by a marked fall in the pulse rate, a diminution of the tremor and an increase in weight.

"This initial improvement, however, *seldom amounts to a cure.* [Italics mine.] The exophthalmos usually persists for months or years. The heart remains irritable, the pulse becoming rapid with exertion or excitement and at irregular periods *we may expect acute exacerbations of toxic symptoms,* which may alarm both the patient and the surgeon."

The reader has already observed that I consider exophthalmic goiter a morbid process belonging strictly to the realm of the internist. Surgery in the usual, ordinary, everyday case of exophthalmic goiter is a fallacious procedure, as pointed out in another chapter. To exemplify, the author can do no better than to cite the following case:

Mrs. A. C., aged thirty-five, appeared in my office January 3, 1919, suffering with typical evidences of hyperthyroidism. *Chief Complaints*: Marked weakness and loss of weight, bulging eyes, extreme nervousness, palpitation, insomnia. *Family History*: negative. *Social History*: married eight years ago; has one child living and well; no miscarriages; menstruation normal; partakes moderately of meats, tea, coffee, and the condiments. Is obliged to do most of her own housework, but obtains a sufficient quantity of rest. *Previous Medical History*: presents nothing of importance, excepting that she had been ailing with evidences of nervous indigestion for some years prior to the onset of present illness and was always more or less nervous and susceptible to hysterical outbreaks whenever worried or excited. *Present Illness*: this began about three years ago, when she began to experience the throbbing sensations of the heart and rapid loss of weight and strength. Her weight, which she claimed was usually about 122 pounds, was at that time 110. She was taken with nervous chills while in bed, and premonitions of physical disaster would keep her awake most of the night. A few weeks after the onset of these symptoms she noticed that her neck was becoming swollen in front and that her eyes began to bulge forward. She consulted several physicians but became progressively worse, and finally, nine months after the onset of these symptoms, her weight having been reduced to 85 pounds, she consented to an operation. Tryroidectomy was performed under the most trying circumstances, for her heart was so rapid and her vitality so extremely low that little hope was held forth for her recovery. After a hard battle for existence, she rallied and made a good surgical recovery within three weeks. Careful postsurgical treatment resulted in a marked improvement of the patient's condition, reducing the heart rate to almost normal, improvement in the exophthalmos, and an increase in weight to 120 pounds within three months. Her physician thought at that time that a complete cure had been accomplished. The dream of complete restoration to health was soon shattered by a recurring sensation of fullness over the thyroid area. This became more and more prominent, and accompanied by an increasing sense of weight, tenderness, and occasionally pain. She returned to her surgeon, who immediately proceeded to operate, discovering a cyst-like mass corresponding to the isthmus of the thyroid gland, about the size of a goose egg. As enucleation seemed impracticable for anatomic reasons, the cyst was incised and drained, the fluid containing a serosanguinous material which on microscopic examination revealed numerous red blood corpuscles, a moderate number of leucocytes especially lymphocytes, and pus cells. Draining was necessary for six months, at the end of which time the wound closed. While this was going on, the Basedowian syndrome gradually reappeared; the gradual loss of weight and strength reduced her to 100 pounds; the exophthalmos, tachycardia, nervousness, tremor, all returned to a greater or lesser extent, and the patient was now in nearly as poor a condition as before the primary operation. She was sent to a health resort for a few months, where she again seemed to gain back her health, the weight returning to 124 pounds with a universal amelioration of all her symptoms. She remained practically well and comfortable until three months ago, when, one by one, her former symptoms began to return, and at the time of her appearance in my office, she presented once more a typical picture of Graves' disease, with the exception that the exophthalmos is not noticeable excepting on close inspection. Her weight is 90 pounds, the heart rate is 104, there is a soft, blowing murmur over the apex, systolic in time and transmitted some distance toward the left axillary space, fine fibrillary tremor of the outstretched fingers, and marked nervous irritability.

The foregoing case is merely one instance of many similar kind which could be brought to light, proving the fallacy of surgery in the *usual* case of exophthalmic goiter.

3. *Duration of treatment* depends largely upon the patience and perseverance possessed by the physician in charge and bears strongly upon the course and prognosis of the disease. The duration of treatment necessary to effect cure is variable. As a general rule, we may state that a case of two or three months' duration usually requires the same duration of treatment; one of a year's duration may require from eight to twelve months. A patient having suffered with hyperthyroidism for a year and a half or two years is more difficult to bring around to a state of permanent clinical recovery, for there has been established a habit, so to speak, of hyperexcitability of the circulatory and nervous systems, with a degree of damage to the organs and tissues so overexcited. Such a case, if successful treatment is instituted, requires from one to two years of careful treatment of a sort characterized by military discipline. Advanced cases, with impending loss of compensation and marked emaciation, are quite difficult to handle, for here we are dealing more with the cardiac than with the thyroid phenomena.

At this point it is well to note that a patient may be considered entirely cured, *i.e.*, restored to his former state of thinking, acting, and feeling, with the possession of his maximum standard of happiness and his maximum standard of usefulness to self and society, and yet present such *objective* evidences of exophthalmic goiter as a still remaining fullness of the thyroid and some exophthalmos. This does *not* mean that the intoxication has not been completely and permanently controlled. Experience teaches us that some enlargement of the thyroid, especially if the goiter was unusually prominent, is apt to remain for a year or two after all other evidences of thyrotoxicosis have disappeared, to become normal within another year or two without treatment. The same may be said of a state of former severe exophthalmos.

The reasons for this are obscure, but I may venture to remark that the explanation lies more in the theory of a temporary "morbid habit" of the tissues of the thyroid gland and orbital tissues than elsewhere.

4. *Environment to some extent alters the progress and prognosis of this disease, and in some instances this may assume an importance equal to that of the question of surgical versus nonsurgical treatment.* Should the patient be sent to a hospital? Should she be sent to a sanitarium? Is it preferable that she be sent off to an appropriate health resort? Or would this patient fare best at home? The answers to these questions can only be decided after careful study of the individual case. To confine oneself to hard and fast rules embracing the management of all cases of hyperthyroidism is to court disaster. These patients are of singular individuality in their existing condition. Their petty whims and notions, the various idiosyncrasies of their personality are so easily brought to the surface that they are influenced by the slightest like or dislike of the doctor, attendants, and last, but not least, the environments in which they are placed for treatment. It has been well said by competent observers that psychotherapy should play an important rôle in the management of exophthalmic goiter, and we can not help but concur and emphasize this matter here.

The hospital, though advocated by some as a routine procedure in this disease is not the place of choice in the average case, unless the patient is menaced by an impending loss of circulatory compensation. Of course, a marked cardiac dilatation requires complete rest in bed, preferably in a hospital, whether there be hyperthyroidism or not, for in such a case the heart treatment is of primary concern. In most other cases, however, we find that hospital treatment is inimical to real favorable progress.

Should we send the patient to a sanitarium? Yes, if the place is one abounding in home-like atmosphere and not approximating in appearance and tendencies the usual hospital. No, if the sanitarium smacks of the usual sickbed flavor, and there are many persons about our patient who are in a helpless condition. Certain subjects of exophthalmic goiter whose chief manifestations refer either to the nervous system or the circulatory apparatus, may do well in a properly managed sanitarium conducted with a strict discipline, yet possessing practically all the qualifications of the judicious sympathy of home-like attributes.

Should we send our patient off to another climate? We can not answer this question without much reserve. Some patients are benefited, others harmed by a trip to a locality possessing different climatic conditions. Perhaps a majority of patients had better not venture forth into a different locality until after all the manifestations of the disease are gone, and then the patient may go where she pleases,—on a vacation, as it were.

Should we keep our patient at home? Yes, in almost every instance, for to remove the patient from her accustomed environments will, with an occasional exception, accentuate the nervous irritability and other symptoms. Of course, strict individualization is here to be observed as in other phases of the treatment of the disease. Where the patient is not in harmony with the home environments, or, *per contra*, where there is a relative who is in constant disagreement with the patient, or in households where tactless, oversympathizing "friends" are permitted access to the patient with the usual deleterious results, the home is by far not the place for our case. But a sane household may be so brought under the sway of the diplomatic physician that it could be favorably modified to act in perfect accord with the patient and in perfect harmony with the various branches of treatment formulated, especially that phase of it which concerns psychotherapy. The atmosphere as thus implied, deserves primary consideration in an outline of the nonsurgical treatment of exophthalmic goiter.

5. *The personality of the physician can not be ignored as a factor in the course and prognosis of a disease in which psychotherapy is a constituent of the regimen.* Coldness or frigidity of demeanor, a stern, gruff, countenance, will be interpreted as lack of interest and must result in failure of accomplishing the purpose in hand. Patience, tact, diplomacy, forbearance, a kindness modified by unyielding firmness, a sympathy not overindulgent, an optimism which shines forth with a radiance enveloping the patient with smiles and cheer, a funny story causing the sick one to forget herself in an uproar of laughter resounding throughout the household, and last, but not least, a sincere, hearty handshake on greeting and leaving the patient,—all these make for improved nerves, sound sleep, healthy appetite, good digestion, rapid improvement and favorable prognosis. All these spell psychotherapy as it is to be applied in the treatment of exophthalmic goiter.

It is evident, then, that the course and prognosis of exophthalmic goiter is as much in the control of the physician's equipment, depending upon his skill, diligence, tact,—in a word, his *expertness* in the use of remedial measures, including psychotherapy, as upon all other factors combined. It is not saying too much to remark that the physician managing a case of this sort, as a captain of a ship on the high seas, may permit his charge to drift on to complete wreck or steer it to complete safety, depending upon the breadth of his experiences and the insertion of his personality and conscience into this vital duty.

CHAPTER X

THE NONSURGICAL TREATMENT OF EXOPHTHALMIC GOITER

Introduction

By the nonsurgical treatment of exophthalmic goiter is here implied the various therapeutic measures to be employed—namely, prophylactic, hygienic, dietetic, medicinal, electrotherapeutic and psychotherapeutic in nature, in contradistinction to the usual *surgical* treatment which includes operative procedures directed against the thyroid gland, the great vessels of the neck, the cervical sympathetic and the thymus. That the nonsurgical treatment is successful and surgical procedures are futile is amply illustrated elsewhere in this work.

However, the term nonsurgical is not used without qualification, though the conditions about to be mentioned, in which the knife is to be used, by no means weaken our premises against surgery in exophthalmic goiter. As pointed out in the chapters on pathogenesis, certain abnormal conditions of the mouth, upper respiratory tract, intestinal tract and female pelvis may instigate an endocrine process expressing itself in thyroid hyperactivity and the Basedowian syndrome. Now the removal in these cases of nasal polyps, diseased tonsils and adenoids, a chronically diseased "controlling appendix" or an inflamed portion of the female pelvic organs may cure the patient of hyperthyroidism. In cases of this sort surgery is sane, logical, and curative, based upon proper scientific deductions. How absurd it would be to perform thyroidectomy in these subjects! Again, we admit the virtues of surgical procedure in instances of secondary or "Basedowified" goiters in which the symptoms of Graves' disease are superimposed upon a simple or nontoxic goiter of some years' duration. Here we are not dealing with a primary hyperplastic goiter of true Graves' disease, and the removal of the tumor mass constituting the original "simple" goiter is the sensible thing to do, preceded by and followed by the proper nonsurgical treatment calculated to overcome the existing symptoms. Again, malignant changes in the thyroid and dangerous pressure symptoms call for thyroid surgery, but it must be emphasized that these rarely, if ever, occur in a primary hyperplastic, true state of Basedow's disease. So that, despite our qualifications of the term "nonsurgical," it still stands out distinctly as indicating a prohibitive attitude against the usual surgical procedures in cases of *primary* exophthalmic goiter.

A patient suffering with such a progressive disease as exophthalmic goiter requires early diagnosis and prompt interference,—treatment directed toward elimination of thyroid products from the blood and curbing of excessive thyroid secretion before serious permanent damage is affected in the nervous and vascular systems. In this connection it is well to remember that many patients having gone the rounds of clinics and doctors' offices, discouraged through tardiness or absence of symptomatic relief, resort to the alluring snares of osteopaths, chiropractors, Christian Science "healers" and the various other cults which have no right to handle such morbid conditions, and finally die of heart failure, tuberculosis, exhaustion, or during an attack of insanity. The first principle, then, is an early diagnosis,—the earlier the better; the second essential is the use of *properly* selected therapeutic measures employed by the *properly* equipped and *properly* inspired medical attendant, for the *proper length of time.* Here it must be remarked that the patient should be made to understand that the disease is chronic, requiring chronic treatment. In other words, the safest plan to pursue is to keep the patient under observation for the same length of time as the previous duration of the illness. The patient must further be impressed with the vital necessity of carrying out all orders religiously, and that her only salvation lies in a faithful confidence in methods employed and an unqualified attention to details. Having succeeded in obtaining the solemn promise that she will cooperate in every possible way without any equivocation, we proceed to the methods indicated by the exigencies of the case.

As in the truism that in no other class of cases do we see so many variations from the standard description as in instances of hyperthyroidism, so it must be concluded that in no other class of cases is individualism as essential a guiding factor in the treatment of subjects of this affection. In every discussion of its treatment, whether it be the hygienic, dietetic, medicinal, electrotherapeutic, or what not, it is well to be guided by the existing indications, leaving always in mind that "what is one man's meat is another man's poison." While one patient may feel better with the use of cold baths another will become nervous, but improve under the influence of tepid tub baths; one patient will improve on an ample beef diet, another will retrogress under the flesh diet of any sort, but improve very rapidly under a vegetarian regime. A vivid example in this connection is seen in iodine therapy. Most patients are made worse by the iodides in any form, yet in the experience of many able clinicians iodine has yielded brilliant results in Graves' disease, and 2 of my own cases attest the virtues of this treatment in isolated instances. In electricity, some are benefited by the galvanic current, others by the static, still others by the sinusoidal, and yet another class by the high frequency current. X-ray treatment also is not at all immune to uncertainties in results; while a considerable percentage of cases are improved by x-ray exposures of the thyroid or of the ovaries, others are not so influenced, and still others are made worse. The armamentarium of the physician must be ample enough to enable him to try out other methods or drugs if the first is found lacking in virtues, until he finds a combination of measures exactly suitable to the case in hand. Any therapeutic remedy or combination of remedies capable of reducing the thyroid secretion to normal without devitalizing the bodily forces is the proper procedure in the treatment of exophthalmic goiter. The combating of symptoms *per se* (tachycardia, nervous excitability, exophthalmos, hyperidrosis, etc.) important as this may be, is a secondary consideration.

However, the circumstances of therapeusis and individualization are not as vague and uncertain as appears at first sight. Let us here emphasize an important fact repeatedly proved by the experiences of many noted men herein cited, and by my own experiences. Every case of exophthalmic goiter (if not yet moribund) is curable by nonsurgical measures of one sort or another, and although there are no real "specifics" in the therapeutics, certain measures act in a fashion specific enough to yield relief and permanent cure in the vast majority of cases.

Since the prevention of disease is quite as important a matter as treatment, the first division of our discussion of the treatment of exophthalmic goiter refers to the prophylaxis of the affection.

I. Prophylaxis*

Since all thyroid enlargements are either toxic or potentially so, it would be well, in consideration of the prophylaxis of exophthalmic goiter, to deal with the question in the broad aspect, *i.e.*, through a discussion of the prevention of goiter in general. The need for this means of approach is emphasized by the fact that many apparently primary etiologic factors are common to both toxic and nontoxic goiter, and also by the well-recognized picture of an old standing simple or "innocent" goiter suddenly evincing toxic manifestations,—the so-called "Basedowified" goiter.

It would not be presumptuous to claim that the prophylaxis of goiter, if earnestly attempted, would succeed in its purpose in from 30 to 50 per cent of instances. Deducting the percentage of cases of hereditary and "idiopathic" etiology, the attributed causes of thyroid enlargements are eradicable, all things being equal. This is attested by experimental evidences not only in goitrous districts of Switzerland, France, Italy, India and elsewhere, but in regions where goiter is not at all endemic. Marine and Kimball, after extensive experiments in this work, conclude that simple goiter is probably the easiest of all known diseases to prevent.

---

*This section, slightly modified, appeared as an article entitled, "The Prevention of Goiter" in American Medicine, April, 1919.

With respect to the causation of goiter, McCarrison thus sums up the question: "The problem of the causation of goiter is one which has exercised the minds of observers since the earliest days of medical history. There are, indeed, few diseases about which so much has been written and so many diverse views propounded. The association of goiter with mountains has led to the promulgation of many of these views. A causal influence has been attributed to the configuration of the soil, to waters derived from certain soils and charged with certain chemical ingredients, to altitude, to the rarity of the atmosphere, to cold and dry air, to air holding too little oxygen and to air holding too much, to air laden with sulphurous vapors, to the action of cold air on the neck, to a want of iodine in the air, to air charged with electricity, and to some half hundred other such causes. One is apt to dismiss with scant ceremony the observations of earlier observers in this field of research, but if we consider some of their views in the light of our modern knowledge of the thyroid function, we shall realize the truth that is in many of them. The effect of altitude and of rarified atmosphere falls into place with the gland's function of regulating the respiratory changes and of maintaining the red blood corpuscles and the hemoglobin at a level proper to the altitude. The lack of iodine in the air at altitudes above 1000 feet will indirectly influence the thyroid toward hyperplasia by its lack in the food. The ingestion of waters charged with an excess of lime adds to the burden of the thyroid's numerous duties. Even configuration of the soil by favoring the entry of surface drainage into unprotected water supplies, is not without considerable influence in the genesis of the disease."

Let us discuss briefly a few of the most plausible views in etiology and prophylaxis of this affection (i.e., simple goiter).

Heredity plays an important rôle in the occurrence of goiter, the percentage of cases so influenced varying widely in the opinions of observers. Female offspring are more influenced by hereditary goiter than male. Moving away to nongoitrous districts tends to cause a gradual diminution of the hereditary predisposition. Billiet, writing in 1835 (quoted by Crotti), remarks that "after emigration from endemic territory the hereditary tendency slowly disappears, a complete cure being effected only in the third generation." It can be surmised, then, that a mother with a goiter may give birth to a child with thyroid derangement, especially if the offspring be a female; also, that the child, though born with an apparently normal thyroid, is more susceptible to thyroid disease than one whose parent's thyroid was normal. The various causes of goiter operating on the mother during pregnancy may similarly affect the infant.

Despite certain recent views to the contrary, the opinion that goiter can be produced by water is based upon more than mere theoretic speculation. From the days of antiquity until the present time, proof is not lacking in order to convince the most skeptical of the causal relationship between certain kinds of water and the incidence of goiter. To pass on from the allusions made on this subject by Hippocrates, Aristotle, Pliny, and others, Lombroso, quoted by André Crotti, alludes to the wells in Cavacurta in Lombardy as, "The goiter fountain which is visited by youths at the time of conscription in order to acquire this infirmity in two weeks, and thus avoid military service." Many are the instances which could be cited of visitors to goitrous districts, who, having developed an enlarged thyroid, were cured shortly after leaving that locality. This need not be necessary, however, as experiments of competent observers prove that the boiling of water is a sufficient safeguard against goiter, the exciting cause being microorganismal in nature.

Bernhard states that a feature of prophylaxis is the presence of a "healthy" well near every schoolhouse. The water may also be purified by ultraviolet rays, or addition of iodine, or boiling. However, natural sunlight is the best disinfectant, and combined with exercise in free air, is also a prophylactic for the child. A survey of shade dwellers and sun dwellers on the slopes of mountain valleys shows marked differences in constitution, the former being more dumpy in build and phlegmatic, while the latter are slender, lean and lively. Bernhard believes that the favorable influence of solar light in the prophylaxis of goiter has never yet been duly honored. He points out that the intuition of a gifted layman has proved to be superior to the scientific knowledge of his day, and many years ago Balzac saw in absence of sunlight and free air the cause of cretinism. Tourists and those who take cures in Switzerland almost never become goitrous as they naturally visit the country only in the summer or sunny months.

Kocher also advocates modifying the drinking water by addition of a minute amount of iodine. In the endemic foci the children first show signs of goiter after a few months in school; the confinement in school predisposes them to feel the effects of the unknown substance that causes goiter. On the other hand, army service is liable to cause the retrogression of established goiter.

Güttinger reported that in one group of 417 young recruits,—all just twenty years old,—331 showed goiter at the beginning of their military service, but no signs of goiter could be discovered in 146 of them at the close of their service. Of 76 visible goiters all had retrogressed except

21 per cent, and of 138 goiters evident on palpation, only 58 per cent could still be felt by the end of their term of service. These facts confirm the importance of hygiene and outdoor life in warding off goiter. Kocher cited experiences which demonstrate the favorable action of iodine in the earliest phases of endemic goiter, and also the experiences with fishes which developed goiter in certain ponds and whose goiters retrogressed when a minimal amount of iodine was added to the water. He therefore suggests that in endemic foci of goiter the younger school children should be encouraged to drink freely of water prepared with a minute amount of iodine. This, in connection with good ventilation, clothing that does not bind anywhere, regular bowel movements, and plenty of exercise in fresh air will tend to ward off the development of goiter. That good drinking water not only prevents goiter but aids in the retrogression of old goiters, was proved by his experience with Lauterbrunnen water supplied to 75,000 school children in the Bern district. He urges that this water should be barreled for the school children.

McCarrison has carried out a large amount of experimental and epidemiologic research which proves that the prime cause of endemic goiter is a living organism. He bases the above conclusion on the following facts:

(1) In goitrous villages situated one above the other on an unprotected water supply, the incidence of goiter steadily increases from above downward depending upon the increased impurity of the water.

(2) Goiter has been produced in the human subject by the ingestion of the residue left on the candle of a Berkfeld filter after infiltration of goitrogenous water. This residue when boiled does not cause the disease.

(3) The administration of intestinal antiseptics, *e. g.*, betanaphthol or thymol, causes the disappearance of recent goiters in young subjects. Lactic acid bacilli administered daily to recent cases of goiter may cause the complete disappearance of the swelling.

(4) The cure of chronic constipation and intestinal stasis associated with goiter, as by the operation of short circuiting or colectomy, causes the disappearance or marked reduction in the size of the goiter (Lane). This proves intestinal toxemia as the causal agent.

(5) Fish confined in tanks situated one above the other on a single water supply, show an increasing proportion of thyroid hyperplasias from above downward. The addition of iodine or the like has a prophylactic or a curative influence upon the hyperplasia.

(6) The administration to rats and dogs of the scraped deposit found on the inner surface of the water-soaked wooden tanks in which the fish are confined, produces thyroid hyperplasia and goiter. This substance is rendered innocuous by boiling (Gaylord).

(7) Rats, goats, and other animals are rendered goitrous by being fed on fecal material from goitrous and even nongoitrous subjects.

(8) Vaccines prepared from intestinal organisms are capable of causing a disappearance of recent cases of goiter when injected in appropriate doses at weekly intervals.

McCarrison concludes from these facts that the causal agents of goiter are microorganisms inhabiting the alimentary canal of sufferers from this disease, and often of other persons whose thyroids show no actual enlargement, but which, nevertheless, may be in a hyperplastic state. These germs reach the alimentary tract through infected soil or water, and such an infected individual may become the "carrier" of the infecting agents.

The marked influence of diet upon the size and activity of the thyroid gland has been known for some time and has been experimentally proved by Watson and others. A dietary deficient in iodine is capable of enhancing the occurrence of simple goiter; food rich in animal proteids or a dietary rich in fleshy substances increases the activity of the thyroid gland with concomitant loss of stored up thyroid secretion which is thrown in excessive quantities into the blood. It is for this reason that a dietary containing a minimum of flesh, or what is best, an absence of animal foods, is the ideal regimen for subjects susceptible to or suffering from goiter.

It has been emphasized by many observers that iodine, the extract of thyroid gland, or both, administered at the right time in proper dosage, are capable of preventing the formation of simple goiter, especially during adolescence. It is without danger if carefully administered. Roux suggests that it would be useful to have an open jar with a few crystals of iodine placed in each schoolroom, the crystals renewed as they evaporate. The amount of iodine thus inhaled would be infinitesimal and harmless, while during the school year it might act as effectually as the iodine inhaled at the seashore, which generally suffices. At the hospital and polyclinic in his charge he distributes on every occasion small boxwood medallions containing a crystal of iodine in waxed paper.

Marine and Kimball state that from the practical standpoint, the first instance of preventing goiter on a large scale was accidental and in connection with the sheep raising industry of Michigan. Prior to the discovery of salt deposits around the Great Lakes, the future of the industry seemed hopeless; but with the development of the salt industry and its use by the sheep growers, goiter rapidly decreased. The explanation, as furnished by Marine, is that salt contains appreciable quantities of both bromine and iodine, and in places these elements are extracted commercially. The second instance of goiter prevention on a large scale was in brook trout, and the disease was averted in the hatcheries by the use of tincture of iodine added to the water. In a census taken by Marine and Kimball of the condition of the thyroid in the girls from the fifth to the twelfth grades of the school population of a large community in the Great Lakes goitrous district, it was found that 1,688, or 43.59 per cent, had normal thyroids; 2,184, or 56.41 per cent, had enlarged thyroids; and 594, or 13.4 per cent, had well-defined, persistent thyroglossal stalks. The district lies near the southern edge of the goitrous area, and it is suggested that communities near the lakes would show a larger incidence. For the prophylactic treatment the authors selected sodium iodide on the grounds of economy and ease of administration. In all their dispensary experiments with children, the authors used either syrup of hydriodic acid or syrup of ferrous iodide, in 1 c.c. doses, daily for two or three weeks, repeated twice yearly. They arbitrarily selected to use 2 gm. sodium iodide, given in 0.2 gm. doses each school day, for each pupil in the fifth, sixth, seventh and eighth grades; and 4 gm. given in 0.4 gm. doses each school day for each pupil in the ninth, tenth, eleventh and twelfth grades. This was given twice annually about the first of May and December, at the schools, by the teachers or nurses. These amounts of sodium iodide provide approximately 1,700 mg. of iodine for each pupil of the fifth, sixth, seventh and eighth grades, and approximately 3,400 mg. for the ninth, tenth, eleventh, and twelfth grades. The summarized results of a reexamination by these observers, made six months later, of all girls from the fifth to the twelfth grades, show that not a single pupil in whom the thyroid was normal at first and who was given iodine showed any enlargement, while of those not taking iodine, 26 per cent showed definitely enlarged thyroids, and some, moderately large goiters. The treatment, in addition, proved of curative value: one third of the goiters marked "small goiters" disappeared; and one third of those marked "moderate goiters" showed a decrease of 2 cm. or more. Accordingly, the investigators properly remark, a distinct therapeutic effect is clearly demonstrated. Commenting upon these experiments, an editorial in the Journal A. M. A. (December 26, 1918) suggests that these statistical findings are the more conclusive because they represent not dozens but hundreds of carefully examined cases. More than 1,000 girls took the full treatment, the latter being restricted for the present to this sex because during the adolescent period simple goiter occurs more frequently in girls than in boys. The iodide rash prophesied by some critics failed to materialize in any noticeable way in more that 5 girls, in whom it was transitory and uneventful, promptly clearing up when the treatment was stopped. The investigators also now give assurance that there is no danger of producing a toxic condition like exophthalmic goiter under this prophylactic regime, as not a single symptom of this alleged danger from the use of iodide was encountered. Nor was anything different to be expected; for, as Marine and Kimball remind us, the risk of inducing manifestations of exophthalmic goiter from the use of iodine in physiologic doses is exceedingly small, even if those cases in which there were large hyperplastic thyroids, that is, the kind of thyroid enlargement that would permit of the most rapid formation and excretion of the iodine-containing hormone. The extent to which iodine is used in general medicine and surgery and the rarity of the development of signs of exophthalmic goiter is the best index of the danger from its use. Iodine is usually employed in immensely large doses; from 0.2 to 0.4 gm. of sodium iodide daily for two weeks would offer a great excess over the amounts necessary to saturate even the largest thyroids, and probably much smaller amounts would suffice in man, as it has been proved to do in the lower animals.

P. Klinger advocates that at least 2 or 4 mg. of iodine should be given to each person daily in experiments in the prophylaxis of goiter. Any amount less than this is futile. Even this totals only from 1 to 1.5 gm. per year.

Hunziker concludes his long study of the prevalence of goiter in different regions and altitudes of Switzerland by sustaining his theory that goiter is a functional hypertrophy of the thyroid caused by the effort of the organism to make up a deficit in the iodine supply. As the iodine is naturally supplied in the food, goiter is prevalent in regions where the vegetation lacks the standard proportion of iodine. Iodine-containing manure in the regions where goiter is endemic might supply the vegetables with the needed iodine, and thus exterminate goiter. Hunziker, therefore, concludes that the iodine-poor vegetables are what connect goiter with climate and geologic formations. The simplest way to remedy the poverty in iodine would be to have salt made with a small admixture of iodine. A year of such "fertilizing" of human beings on a large scale would go far toward solving the problem.

Kjlstad states that goiter is extremely prevalent in the Telemarken district in southern Norway, southwest of Christiania. In one school at Lunde, 80 per cent of the children have goiter. Most of the goiters are of the atoxic type, and they nearly always subside under iodine. He never noted any symptoms of intolerance in children, but several adults developed symptoms of thyrotoxic action, and one girl of fifteen seemed to have had her simple goiter transformed by the iodine into exophthalmic goiter, although the medication had been moderate and the intermissions long. The iodine seems to act on the hyperplasia of the parenchyma; colloidal nodules and cysts are comparatively little affected by it. The parents must be warned that iodine treatment of goiter takes a long time; too vigorous treatment he regards as dangerous. The dosage he prefers with colloidal goiters is 0.10 gm. potassium iodide every other day for two weeks, and then suspension for three weeks and resumption for two weeks, and so on. With merely parenchymatous goiters, he follows the Kocher method of anointing the goiter with an iodine potassium-iodide salve, using from 1 to 3 gm. daily for two weeks at a time, then suspension for three week periods. Salve is better than the tincture, as it spares the skin. No other treatment or other drugs have proved effectual in his experience. According to Kjlstad, roentgen treatment is liable to injure the still intact portions of the gland. With symptoms of exophthalmic goiter or other signs of excessive functioning of the thyroid, sodium phosphate in a 5 per cent solution seems to give good results—a teaspoonful four times a day, in milk. The basis for this treatment is the antagonism between iodine and phosphorus in the action of the thyroid gland (Kocher). He has often seen the goiter subside under this treatment, especially when the patients gave up work and went to the hospital.

One often meets cases of goiter in young, sallow-complexioned girls. These are the cases which McCarrison has designated as instances of toxemic goiter in which he indicates the pathogenesis of the affection. A combination of causes conspires to bring about an enlargement of the thyroid in these instances. The establishment of menstruation with its profuse, painful periods; the coexistence of a degree of chloroanemia; the stubborn constipation with its autointoxication especially by the bacillus coli communis and its products, and according to McCarrison, a "controlling appendix," i. e., an appendix which by its adhesion to neighboring parts controls the onward flow of ileal contents into the large bowel, producing intestinal stasis, may here be associated. A predisposing hereditary taint, that is, the presence of goiter in the mother, frequently renders the child more liable to thyroid enlargement.

The treatment in these cases is the avoidance of the probable cause or causes. The administration of iodine or the iodides, guarded doses of thyroid extract, proper attention to diet and gastrointestinal tract, complete rest during the menstrual period, and if necessary, the elimination of a diseased appendix or other causes of intestinal intoxication or stasis, are here indicated.

A diseased state of the tonsils and adenoids, because of their contained bacterial and toxic deposits, is strongly potent in the production of goiter, both simple and toxic. In every instance of goiter where such diseased lymphatic structures exist, their prompt removal should be considered of primary importance in the treatment. Often surprisingly prompt results are obtainable. A case of mine recently, a woman of twenty-six, presenting a medium-sized nontoxic goiter of four years' duration, was advised to permit the removal of her diseased tonsils. Within six weeks following the tonsillectomy, the patient's improvement in health was so marked and the size of her neck so greatly reduced as to appear almost normal. A few weeks later she was discharged cured, the thyroid became normal, and there was a considerable increase in weight and strength.

On the other hand, Leonard Williams warns us that enlarged tonsils and adenoids are evidences of thyroid deficiency in some children. Says Williams: "Adenoids and enlarged tonsils occur in children who have an inadequate supply of thyroid secretion. The hypertrophic condition in each case is apparently an endeavor on the part of the organism to supply an internal secretion as nearly allied as possible to the one which is lacking. If the hypertrophy is not very pronounced, and if it has not been very long in evidence,—great enough and protracted enough, *i. e.*, to produce complications, such as disease in the tonsils themselves or in the ears,—then the exhibition of thyroid extract will cause the regression." It is advocated that cases of so-called mental deficiency in children should not lead to an incrimination of the size of the tonsils and adenoids unless the latter be diseased. Williams asserts that this mental deficiency is probably due to the presence of an insufficient thyroid gland, the coexisting hypertrophy of the tonsil and adenoid tissue existing merely to compensate for thyroid deficiency. The lymphatic structures should not be removed until after the administration of thyroid extract for a reasonable length of time has not produced a shrinking of these tonsils and adenoids and an improvement in the mental condition of the child.

During menstruation and pregnancy the thyroid gland swells, in some to an imperceptible degree, in others to the extent of goiter formation. Frequently repeated pregnancies, through repeated stimulation of the thyroid gland, may lead to permanent enlargement of the organ, until, in the course of years, a goiter is formed. Shock and emotional excitement during menstruation and pregnancy render the subject more liable to goiter formation. I cases the judicious administration of thyroid glanc or combined with potassium or sodium iodide, and deavor to tranquilize the patient's environments w ally succeed in avoiding the excessive drain upon t roid gland and averting goiter.

In the prophylaxis of exophthalmic goiter, it is emphasize that since many etiologic factors are c both to the simple and the hyperplastic types of goi avoidance of the known causal factors will serve to hyperthyroidism. It must be remembered that th cause or set of causes is known to excite a mere i in the size of the thyroid gland, as for example, inf from the mouth or intestines, the changes incident berty, pregnancy, etc., this thyroid disturbance ofte the form of an aberration of function, *i. e.*, diminis increased, or more rarely, a combination of the two. over, a previously existing simple goiter may becom and give rise to the Basedowian syndrome. The for suggestions calculated to overcome the etiologic common to both simple and exophthalmic goiter m carried out in the latter disease. Due emphasis m placed upon the importance of eliminating tonsill nasal infections, pyorrhea alveolaris, decayed teet autointoxication from the intestinal tract; suscepti dividuals should be ordered to avail themselves of imum of physical and mental repose during menstr and pregnancy; all forms of worry, excitement, and the like, must be avoided. It has been proved cally that an excessive meat diet predisposes to auto cation, and this in turn, may engender hyperthyr It is therefore suggested that the diet be almost, if tirely, of vegetarian character. The strenuous life of with its complex problems,—its hustle and bustle, it tension, restless sleep and hurried meals, conduces t ous dyspepsia and neurasthenia, and is strongly pr tive of hyperthyroidism. The prophylactic treatment of this class of cases is obvious.

Last, but not least, must be mentioned that state of nervous tension with its necessary accompaniment of thyroid instability which is associated with the undue postponement of the married state. Prolonged engagements are especially potent in the production of a varying degree of hyperthyroidism. The author has met with an example of a most extreme case of hyperthyroidism in a girl who developed these symptoms three years after the announcement of her engagement. A heart-to-heart talk with the couple which resulted in their consent to see each other less frequently and to keep good hours, plus the institution of dietetic, hygienic, and medicinal measures, yielded marked benefit within four months. They were then advised to marry. This was followed by complete cure within six months, and they bid fair to "live happily ever afterwards."

II. Hygienic

The prime factor in the hygienic consideration of the treatment of exophthalmic goiter is to locate a possible unhygienic condition whether intrinsically or extrinsically located, which bears a possible direct or indirect etiologic relationship to the disease. The question of environment, rest, exercise, bathing, air, attention to the proper condition of the gastrointestinal tract, and even the subject of recreation must be included in this category.

Rest.—This is emphasized by all who are called upon to treat this affection. It tends to quiet the impetuosity of the function of the vascular and nervous systems. It aids in the conservation of the patient's energy, diminishing the metabolic processes and retarding the body-destroying forces; it reduces the output of thyroid substance from the gland, thereby diminishing thyroid toxemia; it imbues into the patient a sense of repose which is a vital prerequisite to other therapeutic efforts. But for our purpose we must define the term "rest" before proceeding farther.

By "rest" in exophthalmic goiter, I do not nece mean absolute rest in bed for a protracted period as in the Mitchell rest cure. By "rest" I imply any de variety of activity or inactivity which will "shelf, were, those hyperactive thoughts and actions whi to the continuation of the quickening of the body pr characterizing the disease. I mean by rest anything lessens the activity of the bodily and mental func anything which tends to restore the patient's stan physical and mental equilibrium or poise, whethe rest in bed, passive exercises, occasional dinner attendance at lectures, musicales or baseball game versation, reading, laughing, or what not.

In summarizing the value of rest in connection w discussion of the "kinetic drive," Crile states: "If dividual with exophthalmic goiter could be made to nate like a bear, he would probably come out cur when the driving mechanism, the brain, rests, then ganism as a whole rests; and if the rest is long enou tain pathologic states tend to revert to the normal This is not always the case, however, for in the of rest as elsewhere, individualization is of vital tance, and while a complete rest cure may help one p it may be distinctly harmful to another, as the change of a severe, unqualified, prolonged rest in b a chronically restless creature may be too great a and defeat the purpose in mind. Although the mo portant element in the management of conditions irritation and hyperexcitability predominate, is rest body and of the mind, it must not be mere sleep o reclining, but a prescribed kind of rest outlined ca by the scientific medical attendant, embracing not o matter of rest in the abstract, but, more than th quality as well as the quantity of rest and the variati this same rest which merge into a kind of activity wh latter is indicated.

Moreover, we are dealing with a patient who has lost a considerable fraction of the body weight. What is indicated in a case of this sort? Is it to make the vital functions, especially the digestive organs, sluggish by keeping the patient inactive in bed? In the average case the rest cure rests neither body nor mind. The mind, entirely unoccupied and left to itself, becomes introspective and, as a result, more turbulent than ever; the body, because of this mental state, becomes even less stable than ever. Thus, rather than a reduced tension of body and mind, an increased tension—a tension the strain of which occasionally leads to the breaking point—is induced by the rest cure. Hence, patients who have been kept in bed for six, eight, or ten weeks at a time often leave it in a worse condition than they were formerly. Except in cases of extremely dangerous cardiac insufficiency, I have found complete rest in bed strongly contraindicated in the treatment of Graves' disease. Patients can rest quite as satisfactorily by sitting in an armchair, and surely feel more comfortable and contented. This comfort and contentment, though, at first thought a trivial matter, means the difference between the presence and the absence of a sharp appetite. Moreover, the patient need not be deprived of the pleasure of sitting at the family dinner table and even of a nice slow walk in the open. All these, instead of further devitalizing the patient, as is the case with the complete rest cure in bed, strengthen the circulatory, nervous, and respiratory systems, improve the appetite, enhance the digestion and nutrition, and help the patient to take and assimilate greater quantities of food, thus rapidly increasing the body weight. I am therefore strongly opposed to hospital treatment in the usual sense. The congenial home is the ideal place where proper results are most promptly achieved; and if the home, for some reason, is not congenial or is otherwise objectionable, then a sanitarium with environments as near like home as possible is the next best choice. In the latter instances, we assume, however, that the attendants of the institution possess the qualifications herein implied.

However, where the patient's mentality is such that response to reason is not forthcoming to the satisfaction of the doctor,—instances in which the patient is really suffering with a degree of dementia or melancholia, and in a household which is lacking in proper moral fiber, where its members can not be brought to the point of recognizing the vital importance of strict discipline and indomitable adherence to the doctor's orders,—a nurse or two must be put on the case. The nurse in attendance must be capable of being trusted with a difficult charge; she must have complete control of the patient in the absence of the doctor, notwithstanding what the members of the household may say or think. The nurse must be diplomatic, tactful, kind, and sympathetic, yet firm as steel; under no circumstances must there be the slightest yielding to unreasonable demands of the patient or relatives. At a stated moment, precisely, must the patient retire, and at another precisely stated moment must the patient rise. The bath must be given at exactly this or that temperature; meals must be taken at the very moment indicated by the doctor; their duration and manner of chewing must also be carefully supervised. The transactions of the day, including the afternoon nap, rest, exercise, conversation, reading, light games, etc., must all be under the eye of the nurse in these difficult cases if we would win the battle for health. This rigid plan must be adhered to for as long a time as is necessary to bring the heart beats down to normal, and until the nervous manifestations of the disease have disappeared. Not until then may the nurse be discharged and the patient be permitted to follow the doctor's orders alone.

To conclude the remarks on rest, I find that in the usual case of exophthalmic goiter a kind of medium between the complete rest cure and no rest at all is most productive of good results. My patients are made to retire at 9 p. m. At 7 a. m. a light breakfast is served them in bed, and at

9 a. m. they arise. The remainder of the day is so outlined as to be characterized by pleasant outdoor recreation which in time assumes the form of unexciting exercise. An afternoon rest or nap of an hour or two is desirable in some cases. Where the patient must perform his or her daily duties during treatment, we are obliged to meet the situation halfway and permit the performance of half the accustomed daily work unless this is contraindicated by impending cardiac failure.

Exercise.—Exercise must modify and alternate with rest in the average case of exophthalmic goiter. Of course, where the heart is exceedingly rapid, irregular, or is leaking badly and there is danger of loss of compensation, exercise must not be considered, or if attempted, must be *passive* in character, *i.e.*, in the form of massage. But in the usual case we find that a regime of continued idleness, while helpful for a while, becomes monotonous to body and mind, and does not enhance a restoration to the normal of the various body functions. Moreover, in occasional instances idleness is etiologically related, for in leading to introspection it has caused a susceptible individual to become self-centered, paving the way for a state of nervous instability which finally culminates in Graves' disease. Here, of course, exercise is strongly indicated both as a prophylactic and as a curative agent, and it should soon acquire a character both stimulating to the body and interesting to the mind.

In the usual case, then, after a preliminary state of idleness of from a few weeks to three or four months, depending upon individual circumstances, and after the heart rate has been reduced to 80 or less, certain calisthenic movements are ordered, calculated to restore the normal tonus of the voluntary and involuntary muscles of the body. Walking, at first a short distance, later to be increased to two or three miles once or twice daily, is ordered when the degree of improvement so warrants. Horseback riding and rowing are also useful forms of exercise and are a pastime as well, but must not be overdone. Bicycling is to be prohibited as it is too violent and exciting for the heart. Automobile driving is nerve-racking to most cases of hyperthyroidism, but a slow auto ride with the patient passively seated and driven about by some one else is beneficial. The various calisthenic room exercises, not too violent, with or without dumb bells or Indian clubs, once or twice daily, follow in order, especially in younger patients. It must be emphasized that calisthenics and, more especially, apparatus work of the gymnasium must be permitted cautiously and after due consideration of every detail of the patient's condition, and must be indulged in only under the complete guidance of a medical attendant or nurse, lest harm result. It is better to err on the side of conservatism than to court a return of the tachycardia. Incidentally, piano or violin playing are forms of exercise which are effectual in purpose and practically harmless. Those patients who have already studied one or the other instrument may resume their practice with moderation at an early date unless there be a state of cardiac incompetency.

Deep breathing should be taught the patient and encouraged to be practiced throughout life. If we recall the fact that in exophthalmic goiter there is a diminution of respiratory expansion, and also the fact that in this disease there is often a coexistent focus in or a strong predisposition to tuberculosis, we must conclude that the value of pulmonary gymnastics can not be overestimated. Deep breathing may be begun in all cases, however serious they may be. In the advanced form with cardiac embarrassment, the patient is instructed to try to breathe just a little more deeply than usual, and twice a day, night and morning to take ten or twenty deep "sighs." This will serve the purpose at first. In the usual case, in addition to instruction to throw the chest forward and the shoulders backward and to inculcate a deep breathing habit, the patient is ordered to take a deep breath—deep as possible or to within the point of discomfort. A cracking of the usually unexpanded portions of the lungs will be felt and heard. The breath is held for a second or two, and the process of expulsion is begun, again to the point of discomfort. After a second or two, the excursion is repeated. Twenty or thirty such cycles should be practiced each night and morning, either in the open or before an open window. There is not only a beneficial local effect in the lungs, expanding and strengthening areas heretofore flabby and semidiseased and rendering them less liable to infection, but there is a central effect, that is, improved vasomotor stability, increased appetite, and a restoration of nutritive balance is enhanced.

Passive exercise may be given to all subjects of exophthalmic goiter, in the form of mechanical vibration or massage. The vibrator of a type run by a small motor is easily procurable and serves the purpose very well. Hasebroeck states that vibration exerts the following effects on the circulation:

1. A decrease in pulse frequency.
2. Vasomotor heightening of arterial tension.
3. Increase in tonicity of the heart musculature.
4. Increase in blood pressure.

All these results of vibration are desirable in varying degree in exophthalmic goiter. Moreover, vibration, especially if directed along the spine, more particularly the cervical region, at times creates a sense of well-being more promptly than by any other means, through the ensuing sedative effect on the cerebrospinal axis. Manual massage exerts a similar effect, though not as promptly. Passive exercise should be administered lightly and for a brief while at first and gradually increased, depending on the results obtained and the mental attitude of the patient toward the procedures employed. The salutary efforts of passive exercise are often seen in the calm, refreshing sleep which follows the period of its administration.

Climate.—Climate is not an important consideration here. As in asthma, hay fever, nephritis, chronic rheumatism and other morbid conditions, so in exophthalmic goiter do we find that a climate which benefits one patient may not benefit the next. One patient may feel better at the seashore, another in mountainous districts, still another will find improvement in Florida or in Canada. Generally speaking, it has been found that patients fare badly at the sea shore. We must individualize here as elsewhere, and take into account not only the existing physical conditions, but also the patient's peculiarities and idiosyncrasies. All things being equal, the patient being accustomed to his or her home climate, had better not change. In the absence of irritating factors of a social nature, home climate, home faces, home-made meals, and continued home attachments are far more conducive to desired results than a strange, untried climate, strange, indifferent, and possibly insincere faces, and strange, often questionable meals. However, where the home is conducive to oppressive monotony in the individual, or there exists unpleasantness or friction between the patient and the members of the household, a *change of scene* is obviously highly desirable and often of vital importance.

Hydrotherapy.—In exophthalmic goiter hydrotherapy is a useful adjuvant to other measures. A daily lukewarm cleansing bath is, of course, to be advised in every case; the vasomotor instability of the periphery is thereby improved, and the state of hyperidrosis is benefited. Moreover, there occurs a general sedative effect on the heart and nervous system, especially if the bath is taken just at bedtime.

A cold sponge in the morning may be relished by some patients and disliked by others. The aversion to cold water bathing had better be heeded in the average case. However, the application of cold to a very vascular hyperactive thyroid gland and to a turbulent heart is a valuable procedure; this is accomplished by the use of ice bags or the Leiter coil. The slowing of the heart rate is very gratifying to the patient, and the restlessness is considerably reduced. W. J. M. A. Maloney states that wet packs for one hour, combined with the cold Leiter coil to the spine, and followed by a half bath, 79° to 75° F., sometimes allay the tremor and palpitation.

Solomon Solis-Cohen, in discussing Graves' disorder as a form of vasomotor ataxia, states that one of the most potent influences in controlling the symptoms is the reduction of the central and peripheral vasomotor mechanism by means of alternate hot and cold applications to the surface of the body. Says Cohen: "There are many ways of doing this. The simplest, and in the case of patients under absolute rest treatment the best method is, after a preliminary cooling of the head and neck, to sponge the entire body rapidly with water as hot as can be borne (in the neighborhood of 108° to 112° F.), and to follow this immediately by what is called 'a cold friction rub' with water as cold as can be borne; which may be only 80° or 70° F., but later as low as 60° to 50° F., or, in rare instances, even ice water. The whole process, including the final drying with a rough towel, should not take longer than five to eight minutes. Here again, however, there are numerous modifications to suit the individual condition and the individual reaction. Also, in the progress of the case, the time and the temperature, and the method of the applications must be adapted to their effect, on the one hand, and to the new conditions, on the other. Hot and cold packs, sprays, douches, momentary plunges, and the like, are also applicable; the details being modified, of course, by common sense. It is well to instruct the patient to continue the hot and cold sponging or spraying throughout life; to make it a part of the morning toilet, altogether independent of the ablutions of mere cleanliness."

The drinking of an ample supply of cold sterile water should be encouraged. Although in many patients the thirst is excessive, keeping pace with the hyperidrosis and polyuria, in some instances the subject does not imbibe the necessary quantity, as a result of which the functions of the emunctories are hindered, and the emaciation becomes more marked than ever. These patients should be encouraged to take plenty of fluids in the form of milk, buttermilk and an abundance of water.

Gastrointestinal Hygiene.—This subject will be discussed in detail under the dietetic treatment of exophthalmic goiter. The condition of the mouth must be made as perfect as possible. Decayed teeth, pyorrhea alveolaris and the like must be attended to at once and in an expert manner. The patient is instructed in the proper use of the tooth brush, and advised to use a mild antiseptic mouth wash and gargle two or three times daily, and oftener if necessary. Food must be "Fletcherized," and all mental tension must be guarded against during mealtime. A funny story, congenial companionship and other circumstances of like nature enhance appetite, improve digestion, and make for general improvement, especially of the circulatory and nervous phenomena. After food is taken, an hour's rest in an armchair, during which the mind is entertained by light reading, pleasant conversation, light table games, or appropriate music, may be followed either by a nap or a slow walk, as indicated.

The bowels must be kept in good functional condition. The use of drastic cathartics is inadvisable; sodium phosphate is the most useful of laxatives in these cases, if needed.

Mental Hygiene.—Mental hygiene is discussed under psychotherapy. It need only be stated here that all factors conducive to a state of excitation of the emotions are promptly to be eliminated. This concerns not only intrinsic factors such as doubts, suspicions, obsessions, business cares, religious, marital, or sexual matters, but also the various extrinsic factors, as false friends, unsympathetic parents, noisy children, curious neighbors, a jealous, scolding helpmeet, an insipid, unbearable relative, and even stubborn creditors,—all of which maintain a state of discord or friction between internal relations and external circumstances. The importance of a proper understanding of the patient's psychic construction by the doctor and the medical attendants, and their ability properly to employ the necessary psychologic methods in efforts at a restoration of the patient's nervous stability, are highly advisable circumstances in the management of these cases.

III. Dietetic

As in tuberculosis, diabetes mellitus and other diseases where the destructive metabolic processes overbalance the constructive forces, so in exophthalmic goiter the questions of quality and quantity of food and the regularity and frequency of its administration are essential requisites to a restoration of the nutritive balance.

The great loss in weight and strength in hyperthyroidism is due largely to the increased oxidation occurring within the tissues,—the proteids, carbohydrates and fats. This is evidenced also by a rise in temperature and an increase of approximately 60 per cent of CO_2 from the lungs. In addition, the symptoms of indigestion,—the anorexia, nausea, vomiting, diarrhea, polyuria and hyperidrosis further reduce the body weight through a diminished intake of food and the great loss of fluids. The increased metabolism of nitrogen, calcium, sodium and phosphorus, the increase in urea and uric acid, the glycosuria,—all attest the presence of widespread, practically universal loss of material occurring in these patients.

Lichty states that to express it in a concrete way, we can say to the patient who has thyroid disorders, that if 2,500 calories in his food are sufficient to carry him along under ordinary circumstances, with his present condition it will require 4,000 calories. That is, the basal metabolism is increased possibly by 75 per cent. A recognition of this fact will carry us along very far in the recognition of treatment.

The metabolism is increased in hyperthyroidism, and it is therefore obvious that the food must be increased to keep pace with the increased oxidation. In nearly every case of hyperthyroidism, however, the destructive ph metabolism is so great that patients can not take as food as is necessary to maintain the body weight. there is the rapid loss in weight and strength. T creased appetite observed in some cases is merely a n attempt to compensate for this disturbance of met equilibrium, but is insufficient.

With regard to the dietary management of exopht goiter, from a practical viewpoint, the following gener may be drawn:

1. A case of exophthalmic goiter is one of careful, tific feeding without which other measures are of or no avail.
2. The intake of food must correspond in caloric not only to the quantity necessary to overcome to exc oxidation, but must extend beyond that point;—th must be capable of causing an increase in weight to t tient's former standard of avoirdupois.
3. An increase in weight in the patient is an *in* *general improvement* and occurs conjointly with an lioration of tachycardia, nervousness and a feeli well-being.
4. Since many cases suffer with digestive difficult is necessary to institute medicinal treatment calcula rectify the digestive capacity.
5. In order to avoid the condition of "overloadin the digestive organs by the increased daily intake of the administration of six partial rather than thre meals a day is an efficient method in the usual case.
6. The diet must be nearly or entirely nonflesh in acter.

By careful, scientific feeding is meant the ad tration of an ample quantity of highly nutritious irritating food prepared in a palatable, appetizing fa to be taken at properly regulated intervals of time. riety should be the aim in order to avoid monotony. not always necessary to seek far to add to the vari foods. Eggs may be prepared in a dozen or more ways, each constituting a *variety* as far as the eye and taste are concerned. The same may be said of potatoes, noodles, cheese, fruit and even milk. Variety may be a stomach factor, but it is even more a psychic factor, and if the same egg or potato or cheese is prepared in a different way than ever before and the taste partially disguised, and if this dish is made good to look upon and of unusual palatability, we are giving the patient a new dish and increasing his food intake. It is therefore necessary to know something of the culinary art as well as dietetic science, if we would succeed in having our patient fully cooperate in the battle to overcome the metabolic instability and recover.

With regard to caloric value in feeding, a mistake is often committed which should be avoided in cases of exophthalmic goiter especially, and that is, the placing of these patients on a milk diet exclusively as a routine procedure. That a milk dietary is not a desirable means of maintaining the body weight is seen in the fact that even in typhoid fever it has been abandoned in many quarters, with happy results. What are the objections to the so-called milk diet? (*a*) Many patients possess a natural aversion to milk; (*b*) it in time becomes monotonous to nearly every patient; (*c*) it is not really a "complete" food for adults, which fact assists the process of emaciation already being carried on by the existing toxemia, thereby reducing the patient's resistance to a minimum; (*d*) hard, cheesy curds resulting from the ingestion of milk are largely responsible for the irritation of the gastrointestinal mucosa, fermentative processes and tympanites; (*e*) a prolonged milk diet renders the digestive processes so delicate as to lessen their ability to digest other foods for many weeks. This last factor explains why patients under a milk diet, when given more liberal feeding at any time during the course of the disease, fare badly, and often promptly present evidences of digestive disturbances. It is necessary to administer more than 5 quarts of milk daily in order to furnish a sufficient number of calories to maintain the patient's nutrition. This quantity of milk is practically impossible for a person in health or disease, so that if the milk diet is insisted upon, the patient is slowly starved while combating a prolonged metabolic dyscrasia, during which his resistance and nutrition should be safeguarded in order to enhance prompt convalescence and recovery.

Milk *is* a very useful food, but not as the sole article, merely as a supplement to a varied mixed dietary. The same is to be said of the continuous "milk and egg" dietary which, formerly so popular, is now happily falling into disrepute as a cure-all in conditions requiring an abundance of nourishment. Milk and eggs are highly useful adjuvants or supplements or constituents of a varied dietary and serve to fulfill all the requirements of food to be employed for forced feeding. To employ any one or two articles of diet to the exclusion of all the rest fails in its purpose in the great majority of cases.

The very best sign in the world that our treatment is just right is a material improvement in weight, and this, as already intimated, can not be accomplished without dietary considerations. No matter what we do for the patient,—no matter how careful, how skillful we may be in therapeusis, if the weight is at a standstill or only slightly improved after a few weeks' trial, the struggle will be a difficult one, to say the least. On the other hand, we might say that *all means of endeavor should have as a prime object a rapid restoration of the standard weight of the individual.* If this succeeds, the treatment succeeds, and the patient recovers. A gain of 5 pounds, let us say, is almost always associated with a reduction of the heart's rate by at least ten beats per minute; the subjective cardiac distress is reduced; the expression becomes less anxious and more hopeful, the entire demeanor is one of a degree of renewed confidence in the future. The patient looks forward to meal times, sleeps better, arises in the morning less fatigued and more refreshed, and in general everybody sees a change for the better. Thus we have accomplished the first definite step toward victory, and the patient bids fair to make uninterrupted progress until completely well,—restored to happiness, utility and longevity. A patient who responds promptly to a properly outlined regime should gain an average of 2½ pounds a week during the first month, after which time an average of 1½ or 2 pounds a week can be expected for several weeks until the weight is restored to the normal figure. It usually requires from twelve to twenty weeks to regain the former standard of weight. The increase is at first rapid, soon becoming much slower as the normal figure is approached. Occasionally a patient may gain at the rate of 4 or 5 pounds a week during the first three or four weeks, then remain at a standstill for a week or two, after which an increase of a pound or two a week continues until the normal figure is reached. Very often the weight continues to increase to above the normal figure, and it is not uncommon to find that the discharged patient weighs 5 or 10 pounds more than ever before. All this presupposes the existence of a good digestion,—a digestion capable of coping with an intake of a much greater quantity of food than has been the custom of the patient to ingest.

But in the presence of symptoms of nervous indigestion —such troublesome factors as nausea, persistent vomiting, pyrosis, diarrhea, abdominal discomfort and the like, what are we to do? The question of weight must wait upon a good appetite and a correction of the symptoms mentioned, as the food administered acts as an irritant rather than a restoring agent. As a matter of fact, we often find that a patient's chief complaints and the main obstacle to improvement are referable to the gastrointestinal tract. Without a normal assimilation of food, how can we appeal to the reconstructive forces for aid,—how can we expect to obtain a restoration of the functional balance between the organs responsible for the Basedowian syndrome?

The chief digestive difficulty in exophthalmic goiter is a state of nervous dyspepsia,—a functional condition participating in the symptom-complex presented by the and largely due to the peculiar nervous makeup cha izing the Basedowian subject. The appetite vari though there is but little desire for food, as a rule, other hand the patient may have a voracious appeti the food either does not stay down or causes sufferin it does. In a percentage of patients, the periods of a alternate with periods of hunger, vacillating with th ing and waning of the emotional instability.

Of course, it is recognized that all this is of nervo gin and would improve on the amelioration of the But the continued digestive disturbances, a *result* nervous status, have also become a *cause* of it, and we break this vicious circle by attention not only nervous system, but also to the digestive organs dire that more food is tolerated, we will fail in our p Often both therapeutic indications can be accomplish single formula, and in so doing we avoid the imp frequently entertained by the patient that too man cines are ordered.

Though it has often been said that the hydrochlor is sometimes diminished or absent in exophthalmic this is rarely the case. In almost every instance t an excess of acid which if overcome is a relief to tient. In cases of this sort the administration of magnesia, 2 to 4 dr. an hour or two after meals, is o ice. This will also overcome any existing constipati the bowels are still infrequent and fecal retention pected, a teaspoonful of sodium phosphate in a tum of warm water an hour before breakfast every day vised. If diarrhea prevails, we must combine the ma with a bismuth salt. I have found the following pr tion of use in these cases:

℞ Bismuth Subcarb. gr. x
Magnes. Oxid. Ponderos. gr. vi
Ext. Hyoscyamus gr. 1/3
M. et fiat chart No. I. Mitte No. XX.
Sig.: One powder t. i. d. an hour after meals.

Or:
℞ Bismuth Subcarb. gr. viii
Pulv. ext. Rhei. gr. ii
Ext. Hyoscyamus gr. 1/3
M. et fiat caps. No. I. Mitte No. XX.
Sig.: 1 capsule an hour after meals.

In cases where nausea and gastric discomfort are prominent, the following will be found highly useful:

℞ Codein Sulph. gr. iv
Tr. Hyoscyamus ʒ vi
Bismuth Subcarb.
Magnes. oxid. ponderos. a.a. ʒ iii
"Pepsencia" q. s. ad. ℥ vi
Misce.
Sig.: Shake well and take a teaspoonful in water a half hour before and after meals.

In the above formula the bismuth and the magnesia may be increased, diminished, or one of them omitted, depending upon the degree of gastric discomfort and the presence of diarrhea or constipation, as the case may be. The codein in this formula will, to an extent, allay the irritability of the nervous system, but since one might object to it because of its habit-forming quality, we must give it for a short time only, or perhaps substitute the following:

℞ Veronol
Pulv. ext. Rhei. a.a. gr. ii
Bismuth Subcarb.
Magnes. oxid. ponderos. a.a. gr. viii
Ext. Hyoscyamus gr. 1/3
M. et fiat chart. No. I. Mitte XX.
Sig.: 1 powder one-half to one hour after meals.

The following is also efficient:

℞ Taka-diastase gr. v
Veronol gr. ii
Bismuth Subcarb.
Magnes. oxid. ponderos. a.a. gr. viii
M. et fiat chart. I. Mitte XX.
Sig.: 1 powder one-half to one hour after meals.

The ingredients may be varied in dosage according to therapeutic indications. The author can not recommend these veronol-containing prescriptions too highly, a are the most efficient formulæ he has yet employed gastrointestinal disturbances accompanying exopht goiter. In the presence of extreme retching and vo we need but add ¼ gr. cocaine hydrochlorate to eac during the first day or two, after which time it omitted, and as a rule there are no more difficulties direction. The patient now not only retains the fo enjoys it, whereas food was feared formerly because subsequent distress. There is an increase in appeti weight rapidly improves, the nervous symptoms are ually quieted, and sleep becomes refreshing. Of a relapse in the digestive symptoms is always a poss especially when something has occurred to excite t tient in some way. This must not discourage us, ho for as a rule, an extra dose or two of the above form some similar concoction, irrespective of mealtime effort to dispel the cause, will usually overcome th culty, and the patient is again on the road to reco

The administration of six partial rather than thr meals a day, *i.e.*, three *regular meals* without any ef forced feeding and a *feeding* or *nourishment* two o hours after each meal, is the method of choice. Th tra nourishments must not be ample enough to detrac the appetite of the succeeding regular meal; they mu *plement*, not *substitute* the meals and must be given a lar hours. It may be difficult to carry out this plan a as the idea of eating six times a day may not mee the hearty cooperation of the patient, but if the ob is on the score of overfeeding, rather than reduce th *ber* of feedings, reduce the *quantity* of the meal in that the routine be maintained. For example, if taking a medium-sized dinner the patient rebels aga pint of milk two or three hours later, reduce the qu of the dinner the next time, but do not omit the p milk; in the course of a week or two the dinner ne be reduced, for the digestive capacity, with the aid of aments if necessary, will keep pace with the demands of the patient's routine in the dietary.

Milk and eggs as extra nourishments are ideal, but many patients dread the idea of taking these foods, the aversion being more of mental than of gastric origin. I have found that no matter how a patient dislikes milk or eggs, a method of preparation may be found to suit the palate, so that the objection is soon overcome and supplanted by almost a passion for them. Of course, the best way to take milk is to sip it lukewarm, or take it with a teaspoon. In this way it is partly digested in the mouth, becoming more tolerable to an irritable stomach. Milk which would create gastric discomfort, if taken in this fashion, may be imbibed in large quantities with impunity. If deemed feasible, a teaspoonful or less of milk of magnesia or a little sugar may be added. But if the *mind* is made up against these foods, we must employ different tactics. How can we prepare milk to appeal to one who dislikes it? I would advise the reader to try the following preparations:

℞ Cracked ice ℥ ss
Sherry wine or champagne ʒ i-ii
Granulated sugar ʒ i
Pure cream ℥ ii
Cold milk q.s. ad. ℥ viii
Stir and take slowly through a straw or tube.

Or:

℞ Cracked ice ℥ ss.
Granulated sugar ʒ i
Essence of vanilla ʒ ss
Cold milk or milk and cream q. s. ad. ℥ viii
Stir.

Seltzer, if squirted into milk a little sweetened, renders the latter acceptable to some palates. The seltzer must be ice cold and must not be used to excess,—just two or three squirts to the tumblerful of milk. The following combination is relished by nearly everyone, sick or well, as it resembles the usual ice cream soda procurable at the soda fountains:

℞ Cracked ice ℥ ss
Granulated sugar ʒ i
Essence of vanilla ʒ ss-i
Pure cream ℥ i-ii
Cold milk ℥ iv
Seltzer q. s. ad. ℥ viii
Stir and take through straw or tube.

At first one, then two of these drinks are taken at a time. I have succeeded in inducing patients who formerly could not take milk to take three or four pints of the above formulæ between meals. Moreover, it has often been seen that in many instances a person who passionately hated milk has soon been made passionately to like it, and eagerly look forward to the feeding hour.

Eggs may be taken raw, but recent investigation reveals the fact that in this form they are not as nutritious as when soft boiled. However, every practitioner has seen his patients thrive on raw eggs as extra nourishments, when they are not distasteful. Eggs may be soft boiled or poached, or beaten raw with milk or some other fluid. A "milk and egg shake," consisting of a tumblerful of milk with an egg stirred into it, with sugar and vanilla added, is easily tolerated by most patients. Eggs may be beaten up in orangeade or lemonade; in fact, two or three eggs may easily be beaten into an orangeade and administered to the patient who will not even detect the presence of the eggs, especially if the drink is taken ice cold.

Many other methods of preparing milk and eggs may suggest themselves to the mind of the practitioner from time to time, for the purpose of enticing the patient to take these extra feedings. It is highly advisable that when milk is taken, at least a pint of it should be consumed each time. If milk and eggs be taken, there should at least be two eggs and a tumberful or two of milk. In lieu of milk or eggs, a tumblerful of cream may be taken, or two tumblerfuls of a half-milk-half-cream mixture. An extra nourishment may consist of milk toast, *i.e.*, a pint of milk and three or four slices of bread. If buttermilk is desired, a pint or more of it may be taken instead of milk. The same may be said of koumiss and kephyr. The principle of these feedings is obviously the idea of having the patient take an abundance of simple, wholesome, nourishing food, both palatable and acceptable to the stomach. Having prepared the digestive functions for the reception of a reasonable quantity of food, the taking of an *extra* quantity,— the surplus consisting of the above-mentioned substances, soon becomes an easy matter.

The diet in exophthalmic goiter must contain a minimum of animal food. This is attested by laboratory and clinical observations in this country and abroad. By a nonflesh diet is here meant all foods derived from the vegetable kingdom, but including also eggs and the various dairy products.

From a clinical viewpoint, how do the flesh foods compare with a nonflesh dietary?

Flesh foods produce an abundance of purin bodies,—uric acid, xanthin, etc. The intestinal flora contains a maximum of pathogenic organisms; the food is less likely to be fresh, and constipation and autointoxication are common. Flesh eaters are more apt to suffer from digestive difficulties, and extra nourishments are tolerated with difficulty. Flesh food stimulates the physical and mental functions. Now, in exophthalmic goiter, the stomach must be kept free of disturbing elements, and the intestines must be as free from biologic and chemical poisons as possible, and since we are dealing with an already stimulated condition of the body and mind, the stimulation of flesh food is distinctly contraindicated.

A nonflesh dietary, on the contrary, is relatively free from pathogenic organisms and parasites; the food is usually fresh, and if not, is easily detected as such; constipation and autointoxication are rare; the digestive faculties are not hindered, extra nourishments are soon taken with ease, and the body and mind are not stimulated by an excess of purin bodies. It can readily be seen, then, that, in a condition of an already existing toxemia and an already overacting thyroid, no substances capable of further increasing toxemia and thyroid activity are to be permitted. On general principles, the argument resolves itself in favor of a nonflesh dietary.

Strangely enough, most exophthalmic goiter patients are excessive meat eaters. It would not be prudent suddenly and completely to prohibit fleshy food lest the patient weaken from the too abrupt withdrawal of these stimulating substances. In such cases and in instances where it is thought that an occasional chop or small portion of white meat of chicken would exert a favorable influence on the mind, we must compromise somewhat. Care must be taken, however, to avoid the use of the frying pan.

In every case of exophthalmic goiter, a carefully outlined diet list must be given the care-taker, who should be admonished to see that the patient adheres strictly to the foods therein contained. The following lists are recommended:

Partial Flesh Diet List

For......................... *Date*.................

7 a. m.—*Breakfast*

1. Fruit: Orange, grape fruit, baked apple, stewed prunes, bananas and cream.
2. Cereal: Oatmeal, barley, rice, "grape nuts," buckwheat cakes, etc.
3. Eggs: Soft boiled, poached, fried, scrambled, as desired (use no lard).
4. Bread and butter, as much as can be eaten.
5. Beverage: Milk, (hot or cold) "Postum," chickory infusion, or chocolate.

10 a. m.—*Extra Nourishment*

This may consist of one of the following:

a. Two tumblerfuls of milk, hot or cold.

b. Two tumblerfuls of milk prepared in the manner suggested (with sugar, vanilla, seltzer, etc.).

c. Two tumblerfuls equal parts of milk and cream mixture.

d. Two raw or soft boiled eggs and a tumblerful of milk.

e. Milk toast.

f. One tumblerful or more of cream if digestion permits.

1 p. m.—*Luncheon*

1. Steak, chops, fowl, stewed or broiled (not exceeding ¼ pound).
2. Potatoes (baked, mashed, or French fried without lard).
3. Legumes: Peas, beans, lentils (small quantity).
4. Green vegetables: Cauliflower, spinach, cabbage, lettuce, squash.
5. Plenty of bread and butter.
6. Stewed fruit: Apples, peaches, pears, prunes, and the like.
7. Beverage: As at breakfast time.

4 p. m.—*Extra Nourishment*

Consisting of any one of the nourishments enumerated for the ten o'clock feeding.

7 p. m.—*Dinner*

1. Soup: Vegetable, barley, rice, noodle, potato.
2. Eggs: In any form above mentioned.
3. Cheese: Cream or cottage cheese, with or without cream (sweet or sour).
4. Dessert: Bread pudding, rice pudding, tapioca, or corn starch.
5. Fruit: Stewed or raw; apples, pears, peaches, etc.
6. Beverage: As at breakfast.

9:30 p. m.—*Extra Nourishment*

As above mentioned.

Remarks: The above is a mere specimen menu to indicate that it is not at all a difficult matter to arrange meals with a minimum of animal foods. It is necessary to avoid monotony by a frequent change of menu; one may select a few articles from the following list in preparing varied dishes:

Meats: Duck, goose, squab, tongue, sweet breads (not exceeding ¼ pound).

Dairy products: Peptonized milk, koumiss, kephyr, matzoon.

Cereals: Hominy, sago, macaroni, spaghetti.

Vegetables: Asparagus, rhubarb, celery, watercress, beets.

Fruit: *Ripe* bananas, grapes, cherries, plums, dates, figs, pineapple.

Nuts: English walnuts, chestnuts, pecans, hickory, Brazil, filberts, butternuts. Patients must be warned thoroughly to masticate nuts or foods containing them, before swallowing.

Ice Cream: Vanilla, chocolate, peach.

Beverages: Grape juice (sparingly), vichy, lithia water, White Rock, Apollinaris, Poland, Congress.

The following substances are *strictly forbidden*:

Meats: Pork, mutton, ham, sausage, liver, kidney, tripe.

Fish of all kinds.

Soup: Bouillon, and the various broths excepting chicken broth. Also tomato soup, onion, pea, and bean (pea and bean soup may be taken sparingly).

Shell Fish: Including oysters and clams.

Cheese: Schweitzer, Roquefort, and the various spiced cheeses.

Fruit: Unripe bananas, and unripe fruits of all sorts, strawberries, watermelon, blackberries, huckleberries, gooseberries and raspberries.

Fresh breads and pastries.

The various kinds of canned goods and delicatessen.

Condiments: Of all sorts, especially pepper, horse radish, mustard, catsup, and excess of vinegar, sour pickles or tomatoes.

Beverages: Tea, coffee, cocoa, alcoholic substances, an *excess* of carbonated beverages and of beverages containing lemons or oranges.

Where a patient does not seem to require animal food, the diet list should be preceded by the following remark: "All animal foods excluded; in other words, do not eat anything which is capable of eating. Milk and eggs, however, though animal foods, may be taken with impunity."

In the presence of marked glycosuria or even diabetes, one must be careful to use good judgment in the formulation of a diet list. The quantity of acid fruits and sweets and all foods containing a large percentage of starch should be regulated in accordance with the severity of the situation. In marked cases it may even be necessary to employ the starvation treatment of Allen for a brief while, or until the urinary reports become satisfactory. However, we must guard ourselves against extremes in food restriction, for in so doing the ensuing weakness may be so great as to diminish the individual's recuperative powers to a dangerously low ebb. In some instances where the emaciation is very prominent, an excess of sugar in the urine must be ignored. Our chief aim must lie in the direction of feeding up the individual before any attempt is made seriously to curtail the glycosuria. Generally speaking, it might be said that in most cases of glycosuria in Graves' disease it is only necessary to reduce the quantity of sugar-forming foods in moderate degree and correspondingly increase the proteid allowance. In this way, the building up process is not materially hindered.

So far, we have been working toward a definite goal—namely, the attainment of a sufficient increase in weight to correspond to the patient's standard before the onset of the attack of exophthalmic goiter. It is a common experience of medical men to observe a certain amount of loss in weight a short while after having succeeded in assisting the patient to a desired figure of avoirdupois. In order to avoid this possibility of partial relapse in the question of weight, it is well to aim originally at a figure 5 or 10 pounds *beyond* the patient's former standard in order to reassure ourselves. When this standard is reached, we find our patient in a state of practical complete recovery in nearly every instance. By the word "practical" recovery I mean subjective recovery. In other words, with the patient's weight completely restored, there is a dawn of the feeling of well-being which characterizes a complete recovery from a chronic illness, but which means that objectively, though we have attained the victory sought for, we must follow it up for still a few months to a state of permanency.

IV. General Medicinal Treatment

It has often been remarked by surgeons that nearly every drug in the Materia Medica has been tried in the nonsurgical treatment of exophthalmic goiter, with asserted success or failure, as an implication that there is no adequate medicinal treatment of this disease. This is not so. It is admitted that in exophthalmic goiter the drugs to be tried are at times so numerous that the matter becomes rather discouraging to one who has not devoted much time to this subject. The reason for this situation is to be found in the multiplicity of factors bearing etiologically upon the disease. Though the clinical manifestations of Graves' disease have in all cases many things in common, being directly due to the presence of an excess of thyroid substance in the body tissues, the factors leading up to the syndrome are as varied and numerous as there are drugs in the Materia Medica. It can thus be seen that a drug or combination of drugs favorably influencing the symptoms of a given patient does so by correcting the particular etiologic factors, and that the treatment of another case may not succeed by these drugs, requiring something entirely different. It is probable, however, that the majority of cases are due to etiologic factors either identical or quite similar in nature, for there are several medicinal agents which are successfully employed in most instances. Cases which cannot be included in this category are not incurable, for it must be stated that, all things being equal, practically every case of primary exophthalmic goiter yields successfully to one or another remedial measure or combination of measures, depending upon the experience, skill, and perseverance of the attending physician.

Let us consider a few substances of biologic derivation, and then continue on to the various inorganic and miscellaneous substances.

Thyroid Extract.—In the treatment of exophthalmic goiter this extract is mentioned merely for the purpose of condemning it. To employ it in this disease is to pour gasoline over a conflagration. In former years thyroid extract was employed by some, on the supposition that Graves' disease, being a condition of altered thyroid secretion and overwork of the thyroid gland, its use would rest the organ and relieve the symptoms. Alert clinicians soon discovered that in this condition the blood is already overburdened with thyroid elements, and that to administer thyroid is to invite a fatal result. In instances of simple goiter, however, or where a simple goiter bids fair by its presence to give rise to secondary changes, thyroid extract *may* be tried, but very cautiously. I say cautiously, because though its administration may result in improvement of the nontoxic goiter, on the other hand, toxic symptoms may promptly supervene. There is still another instance in which thyroid extract may be tried, and that is, in a case which manifests evidences of *hypo*thyroidism during the course of the Basedowian syndrome. Here also the thyroid substance must be given in small doses at first and its effects carefully watched, while the treatment instituted against the hyperthyroidism must also be continued if the heart rate and other symptoms so warrant. A rare case of survival of thyroid administration in true Graves' disease is no argument for its use.

Parathyroid Extract.—This extract has been found useful at times, especially when there is a suspicion of tetany. It seems to control the tremor and mental excitability. Solomon Solis-Cohen states: "In the medicinal and hygienic treatment of a case of exophthalmic goiter, the patient recovering under these measures may retain or develop certain symptoms, the type of which may be aptly illustrated by the tremor which is considered one of the cardinal features in the diagnosis, and which may possibly, indeed probably, be attributed to compromising of the parathyroids and production of this highly important compound to which our attention has been called. In such instances, I have found empirically, that the administration of parathyroid substance—and I mean genuine parathyroid substa is the best means of controlling such symptoms. The ment was based, of course, on the familiar observatic tetany following removal of the parathyroids and sim to the rôle of calcium in such cases; it is sometimes that the association of calcium bromide or other ca salt with the parathyroid is better than the parath alone in controlling the tremulousness and exciteme these patients."

Pituitary Substance (posterior lobe).—Pituitary stance has been found to yield excellent results in a c percentage of cases. It seems to control thyroid an renal activity, and if not given in excessive doses, see exert a sedative effect on the sympathetic. It is u administered in 5 drop doses intramuscularly, incre to 20 or 30 drops once or twice daily at first. Occasi the results are prompt and startling. Pal reports th of a man who had lost 30 kgm. of weight in a year's Upon admission he showed a tremor of the hands an and was suffering from insomnia, vomiting, diarrhea, nea, and exhibited Von Graefe's sign, a pulsating g and a rather pronounced tachycardia. He was upon a vegetarian diet and given subcutaneous inje of pituitary extract for three months, receiving alto 70 injections of ⅔ gr. each. Under this treatment t tients' weight rose from 46 to 93 kilos, the heart ra from 140 to 92 or 100, the tremor lessened conside sleep returned, and the breathing became easier. Mo cently, Pal reported his observations on 16 cases und same treatment. He concludes that the subcutaneous tion of an extract of the infundibulum part of the pit gland had apparently no influence on the normal thyroi on ordinary goiter, but that it displayed a pronounc tion on the thyroid when functionating to excess, as ophthalmic goiter. The symptoms subside, althoug goiter may increase in size under its influence. Pal that pituitary treatment is able to arrest destructive retrogression in the excessively secreting thyroid.

Hector Mackenzie, Sir James Barr and others have also obtained good results from pituitary substance in exophthalmic goiter. Barr suggests that the combination of pituitrin with thymus extract is exceptionally useful. Another instance of marked improvement with the use of pituitrin is reported by Solomon Solis-Cohen. The case was that of a woman in the Philadelphia General Hospital who had been in the house for more than two years before she was brought to his personal attention. Says Dr. Cohen: "This case was one of moderate severity, with periods of extreme tachycardia, and the exophthalmos was of such a degree that about one-fourth of the eyeball was left uncovered when the attempt was made to close the lids. Intramuscular injections of pituitrin at first in small doses (*circa* 5 minims) and afterward in rather large doses (20 to 30 minims) were given, at first once and afterward twice daily. Improvement, both subjective and objective, was marked and rapid. The heart had become quiet, the goiter was scarcely more than visible, and the eyelids closed almost completely. Such rapid improvement is not the rule. The effect is gradual, but progressive, and the pituitrin needs to be supplemented by thymus or other appropriate adjuvant."

In the presence of marked vasomotor instability with low blood pressure and considerable dilatation of the cervical blood vessels, and in cases in which pituitary and suprarenal insufficiency coexist, pituitrin treatment alone or as an adjuvant to other measures, is highly useful, and should be thoroughly tried out. Pituitary substance is contraindicated in the presence of myocarditis, high blood pressure, and arteriosclerosis.

Tethelin—Tethelin is a substance recently isolated from the anterior lobe of the pituitary body by T. B. Robertson of the University of California. Richter, of St. Louis, and others report very favorable results from the use of tethelin in exophthalmic goiter. While this matter is yet in the experimental stage, it is claimed that this new product pituitary body is capable of controlling the main syn of Graves' disease, favorably influencing the tachy nervous manifestations and metabolism by its antit effect.

Thymus Substance.—Thymus substance has been u Owen, Mikulicz, and many other observers with vary grees of success. It is administered in doses of fro 15 gr. three times a day for months. Thymus is counteract thyroid overaction. Solomon Solis-Coh gests that thymus must be given in doses sufficientl to produce its effects; he often combines or alternat with adrenal substance. On the other hand, O. Pi Madrid states that thymus is contraindicated as it thyroid activity.

Suprarenal Gland.—Especially if combined with extract, suprarenal gland is of decided value in the p of low blood pressure. Sir James Barr has obtaine results with adrenalin in combination with calcium There is strong reason to believe that the supraren stance is a powerful check to the overproduction of elements, as it has yielded some surprisingly good in scattered cases. I have obtained excellent resul the extract of suprarenal gland combined with quin drobromide.

Ovarian Extract.—Excepting in patients at the pause and in cases in which the pelvic organs are su of being etiologically implicated in the Basedowia drome, ovarian extract has proved unreliable. Cor teum has seemed of decided value in early and mil in virgins, in the beginning of treatment, and is sai an antidote to thyroid intoxication. (Berkly.)

H. H. Hoppe recommends, in addition to ordinary treatment, hygienic measures and partial rest, the istration of extract of corpus luteum, 0.12 gm. with hydrobromide, 0.12 gm. and extract of belladonna gm. per dose. He gives nearly all patients the ext corpus luteum continuously,—some once a day, others two or three times a day. As long as this is done he believes that the patient will be improved and can be kept in a fairly normal state. I would state that the relief obtained is probably due largely or entirely to the quinine hydrobromide.

Pancreatic Extract.—Pancreatic extract is of service, especially in cases associated with symptoms of apparent pancreatic insufficiency, *i.e.*, glycosuria, polyuria, bulimia, polydipsia, fat in the stools, etc. Pancreatic extract may incidentally overcome nausea and vomiting, improving the nutrition by correcting starch indigestion. In addition, J. Rogers suggests that pancreatic extract exerts a sedative effect in hyperthyroidism. Chvosteck reports the case of a patient with apparently typical exophthalmic goiter, who showed no improvement under the usual measures. The discovery of large proportions of fat in the stools and an abnormal appetite suggested some disturbance in the pancreas, and under pancreas organotherapy the entire syndrome rapidly changed for the better, the patients soon regaining full earning capacity. The improvement continued as long as the administration of pancreas extract was continued, but the symptoms returned when it was suspended; they were again banished by resumption of the pancreas extract.

Lactic Acid Ferments.—These ferments are employed by McCarrison and others on the theory that hyperthyroidism is largely due to autointoxication. Pietrowicz has observed a marked influence on the Basedowian syndrome by the use of buttermilk and lactic acid ferments from artificial mediums; a considerable slowing of the heart and decided diminution in the severity of the nervous and gastrointestinal symptoms were noted.

Vaccines.—Vaccines derived from a coliform organism grown from the feces of the patient have yielded good results in the treatment of endemic goiter, according to McCarrison, who has had exceptional opportunities of thoroughly trying out this mode of treatment. If this be true of simple goiter, it must succeed in some instances of exophthalmic goiter which depend for the syndrome upon intestinal autointoxication. McCarrison gives this vaccine in doses of from 150,000,000 to 300,000,000 at intervals of from seven to ten days, and has found that five or six inoculations is all that is required to cause a complete disappearance of the swelling. In some recent cases as few as two inoculations were sufficient. Apart from the slight discomfort at the site of inoculation for twelve hours or so, the patient is free to follow his usual avocations. A portion of the skin of the upper arm is painted with iodine tincture and the inoculation made without any further preliminary sterilization of the skin. An autogenous vaccine is on the whole more useful than a stock vaccine, but McCarrison found the latter to act admirably. He says he cannot as yet attribute any specific action to the organism from which the vaccine is prepared. But so far at least as goiter is concerned, the efficacy of a vaccine does not depend on the specific nature of the organism from which it is prepared. He has employed other vaccines and in some cases with surprising results. One patient was successfully treated with a staphylococcus vaccine. The result could hardly be better. The staphylococcus was taken from a diseased femur in a nongoitrous individual. Three inoculations of 250,000,000 caused the bone to heal and the discharging sinuses to close up, while it took five doses to bring about the change in the goitrous individual. McCarrison remarks that the *staphylococcus albus* is certainly not the cause of goiter, yet a vaccine prepared from it can cure the disease.

Serum Therapy.—In exophthalmic goiter serum therapy has had its days of prominence, but, excepting in isolated instances, this treatment seems to be of questionable value. These serums are administered on the hypothesis that they are capable of neutralizing the excess of thyroid secretion in the blood and of overcoming the hyperactivity of the thyroid gland. The bull, sheep, dog, goat, horse and other animals are thyroidectomized and their serums prepared and standardized for administration. Among the preparations employed are:

Thyroidin or *antithyroidin* prepared by Moebius from the serum of the sheep deprived of the thyroid gland six weeks before the first serum is taken. It may be given by mouth, subcutaneously, or intramuscularly. The dose is 10 to 20 drops three times a day for a period of several weeks, when the treatment is discontinued, and resumed some time later if deemed feasible.

Rodagen, the dried milk from the thyroidectomized goats, has been used with asserted success by several observers, and was introduced by O. Lanz.

Rogers and Beebe prepared a serum from two hyperplastic thyroids obtained from an autopsy of Graves' disease patients. They injected these into a rabbit in order that the nucleoproteid might produce a cytolytic effect and the thyroglobulin an antitoxin influence. The serum obtained is administered to patients with varying degrees of success by Rogers and Beebe, who assert that this treatment is not to be employed if the chromaffine system is affected. According to Frederick Forcheimer, this mode of treatment has no reason for existence and should never be used.

Antidiphtheritic serum has succeeded in relieving the symptoms of a few cases of exophthalmic goiter, according to reports. This requires further verification.

Having enumerated the most important biologic products which are identified with the therapeusis of exophthalmic goiter, let us briefly review some of the most important miscellaneous drugs:

Lecithin.—H. J. Berkley has obtained remarkable results from the use of an alcoholic solution of lecithin in the nervous asthenia of exophthalmic goiter. These patients cling to the remedy "as an opium habitué clings to that drug," despite the nauseating and disagreeable odor of the solution, and do not seem to tire of it until the nervous symptoms have been allayed, and the gain in weight approaches the normal. This remedy quiets the nervous irritability and lessens the tremor. In Berkley's experience, some of the patients assert that the tranquilizing effect of lecithin is much greater than that produced by the bromides. To quote Berkley: "The lecithin preparation is a product which in some instances requires careful handling. When there is disturbed digestion it is out of place, and in such an event other remedies that are better suited to allay and restore to its normal condition the disordered alimentary canal, must first be employed. Again, in certain cases, its action should be carefully watched, lest it induce extensive erythematous rashes, to the annoyance and discomfort of the patient. Furthermore, lecithin, *per se,* is an entire failure without the assistance and support of a milk diet. I can recall no instance of its complete success in either asthenia or Graves' disease when milk was not tolerated, and at least one liter must be taken, daily, by the patient. We do not, however, rest on an entire milk diet in these cases, but allow all wheat foods, eggs, raw and cooked, all suitable green vegetables, as well as fruits, and only cut out meats, sweets, and special foods which are known to disagree with the patient; and everyone has his own food idiosyncrasies, which must be respected. Patience, the careful notice of trivial symptoms, as well as their judicious treatment, will repay in the increased comfort of the patient. Though lecithin is probably a constituent of every cell of the body, and especially of the neurons and leucocytes, its action as a medicine is not fully understood. As an erythrocyte producer, with *pari passu* increase of the leucocytes up to 18,000 per cubic millimeter, it has no equal, iron manganese, phosphorus compounds falling far behind it, as is shown in instances of pernicious anemia, chlorosis, and ordinary anemia. As a rule it acts best when hemoglobin is below 70 per cent and the coagulation of the blood is slow. It is also conceivable that lecithin acts as an antithyroid hormone. When the thyroid secretion is overactive there is a progressive loss of body weight—digestion and assimilation being assumed as normal. When the thyroid hormones are in partial or entire abeyance—the same conditions applying—there is a progressive gain in body weight. That an increase in weight follows the administration of lecithin is rather singular when it is remembered that the active constituent is phosphorus, which together with iodine—the peculiar stimulant of the thyroid gland—is usually recognized as an excitor to the secretions of the named gland. Now, we have, apparently, the reverse action, the phosphorus nullifying the activity of the thyroid hormone, or to put it in the vulgate, we find the phosphorus compound stopping the active nervous symptoms in the two maladies, nervous asthenia and Graves' disease, maladies that upon the surface are entirely different in their etiology. The most plausible explanation of its powers is that it stimulates (through the agency of the leucocytes) the resistive powers of the tissues in general to greater activity; probably, also, it increases the secretions of the closed glands, such as the suprarenals and portions of the pancreas, as well as assists in erythrocyte formation and increases the phosphorus content of the leucocytes of the blood."

I administer lecithin in solid form in combination with quinine hydrobromide and other suitable ingredients, and can largely substantiate Berkley's clinical experiences with this drug.

Quinine.—Especially in the form of the neutral hydrobromate or hydrobromide, quinine is the drug *par excellence* in the treatment of exophthalmic goiter. Forcheimer has been obtaining good results with these substances for more than thirty years. He combines quinine in gr. V doses with ergotin gr. I in gelatin-coated pills, to be taken three or four times a day. According to Forcheimer: "The good effects under this treatment usually follow in the same sequence; first, the tachycardia improves, the pulse frequently coming down from 130-140 pulse beats to 80 or 90 in forty-eight hours. Secondly, the thyroid gland diminishes in size, by measurement. Thirdly, the tremor and exophthalmos disappear. In by far the greater number of cases the exophthalmos is the last symptom which disappears; indeed, in a goodly number of patients it never disappears. To convince oneself that the treatment is the cause of the changes just noted, it is necessary only to withdraw the pills and, unless the patient is cured, the symptoms recur. If, after the withdrawal of the pills the symptoms disappear, such patients, as a rule, may be considered cured. Relapses are not uncommon; these patients have relapses on account of psychic or physical irritations and these relapses should be treated in the same way as before. It is on account of these relapses that the disease may last so long. The treatment just described is most valuable in the mild attacks, the percentage of complete recoveries being very large and after a short time. When the fully developed form exists, either primarily or as a relapse, complete recoveries are the rule, but more time is required. When the patient has the foudroyant form the results are excellent."

How quinine hydrobromate exerts its beneficial effects is still a matter for speculation. It has been suggested that "the iodine is counteracted, the sympathetic center is stimulated, there is contraction of the central vascular trunks, reflex sensibility is influenced, leucocytes laden with iodine are checked in their movements, and the elimination of urea is enhanced, while its formation is cut down."

Incidentally, I have seen no untoward effects of quinine hydrobromide on the gravid uterus in subjects of hyperthyroidism during pregnancy. I consider this an important observation, as pregnancy is said to aggravate the thyroid activity, and it is of vital importance to continue treatment as vigorously as ever during that period. The harmlessness of quinine in pregnancy of these patients is due to the great tolerance of quinine evinced by subjects of hyperthyroidism. Quinine hydrobromide (or even the sulphate) may be administered to these patients in doses as high as gr. x or more, t. i. d., with perfect freedom from cinchonism.

Arsenic.—Arsenic seems to exert a sedative or inhibitory influence on thyroid activity in addition to its virtues as a glandular reconstructive, and its general hematinic and alterative effect. It may be used in combination with other drugs, in the form of the trioxide of arsenic in doses of from gr. $\frac{1}{60}$ to $\frac{1}{20}$, or as the arsenate of iron gr. $\frac{1}{16}$ to $\frac{1}{10}$.

Arsenic and Mercury.—In combination arsenic and mercury have yielded good results in the hands of a few clinicians. L. Weber reports the successful employment of arsenic and corrosive sublimate in Graves' disease for their antitoxic effects. He says: "The patient was ordered arsenic gr. $\frac{1}{60}$, and corrosive sublimate gr. $\frac{1}{60}$ in tablet form, to be taken t. i. d., and about one month after the introduction of these remedies she showed signs of improvement in all the symptoms. She continued to take the remedies with but little interruption for nearly three years, recovered entirely and has not been in need of any treatment for the last two years. In 2 other cases which have come under my care since 1903, I have had equally good results from the same remedies; however, they were not severe. I shall be gratified, if this short communication will induce other practitioners to try the treatment in suitable cases." It must be said, in passing, that these reports, though speaking well for this treatment, are not to be taken unqualifiedly. In all likelihood, if a Wassermann test had been made in these cases, they would have been found positive, thus explaining the successes. This is also to be said of the few reports of cures of exophthalmic goiter by the use of *salvarsan* or *neosalvarsan.*

Iron.—Iron may be employed on general principles, in the presence of the usual indications. In the average case of exophthalmic goiter, the anemia is not severe enough to require iron. When it is used, care must be taken to avoid constipation. The carbonate and the pyrophosphate of iron are the most acceptable to the gastrointestinal tract.

Iodine Therapy.—In Graves' disease iodine therapy has been the subject for discussion for many years. It is incontestable that iodine, locally and internally, is ve ful in the prophylaxis and treatment of *simple* goite cording to McCarrison, iodine causes the goiter to to the colloidal state. It also assists in the absorp pathologic tissue within the gland and acts as an ar to the intestinal tract, destroying certain contents might bear etiologically upon the disease. Thus, men in thyroid therapy have succeeded in curing man nontoxic goiters and in reducing the size of quite percentage of old goiters. "Iodine triumphs in th of diffuse parenchymatous atoxic goiter, either mouth or rubbed into the gland as a salve with o iodine to ten parts potassium iodide and 100 parts tum, but always very cautiously and under medical vision. The goiter may increase a little under th ence of the iodine, and it should then be suspende these are the cases that respond favorably to iodi dine may help also in the atoxic, knobby, diffuse form, but if no benefit is apparent in four or six w had better be dropped" (Lanz). The use of iodine i patients is not without danger in a small percen cases. A simple goiter may become "Basedowifie symptoms of which may persist even after the disc ance of the drug, necessitating the institution of the nonsurgical treatment of the exophthalmic type of In commenting upon iodine therapy in thyroid e ments, E. C. Kendall says: "The relation between ministration of iodine and thyroid trouble assumes t tinct conditions: one is the relief of goiter by the a tration of iodine, and the second is the production of thyroid symptoms by the administration of iodine. first condition, the gland is enlarged because it is lated, due to the insufficient amount of its active uent; the stimulus of the gland is, therefore, remov the size diminished, possibly restoring it to norm encapsulated adenoma or a cystic condition is pre mechanical factor enters which does not permit th to return to normal size. The administration of thyroxin in large amounts produces typical hyperthyroid symptoms. It would, therefore, be expected that the administration of iodine in such amounts as to produce an excessive outpouring of thyroxin, would result in hyperthyroid symptoms. Besides these symptoms, due to the active constituent of the thyroid, there is still another condition, known as 'iodinism,' which is a distinctly different trouble. Very small amounts of iodine given to an exophthalmic goiter patient sometimes produce clinical improvement, but it is not a curative measure. The relation between iodine and clinical symptoms is very difficult to explain, but it seems probable that the determination of the functioning groups in the active constituent of the thyroid will throw much light on the subject. It is possible to explain the toxic symptoms produced by the hyperplastic thyroid by assuming that an excess of its secretion is being formed. This can be disproved by the fact that the amount of iodine in the gland is lower than normal, which probably is not entirely explained by the immediate pouring out of the substance from the gland, although this may, in part, be the explanation. Another explanation is that the gland produces thyroxin without the iodine attached. The body would thus be supplied with possibly an enormous quantity of the functioning part of thyroxin, which could theoretically produce the effects that are known."

Halstead has shown that the removal of part of the thyroid in an animal results in secondary hypertrophy in the remaining portion with increased vascularity and increased colloid formation; if iodine is administered soon after operation, no hypertrophy occurs; or if iodine administration precedes operation, little or no hypertrophy occurs. Marine and Lenhart are also convinced that "in the presence of sufficient doses of iodine all true hyperplasia is prevented." They have used iodine in the form of the iodide of potassium, syrup of hydriodic acid and the syrup of the iodide of iron; no untoward effects were noted in the seventeen cases so treated. Moreover, it is an established fact that the vast majority of hyperplastic thyroids contain less iodine than is found in the normal gland; the greater the hyperplasia, the less the iodine content. Theoretically, the introduction of iodine into the system results in a resting stage of thyroid function with consequent opportunity for the restoration of its physiologic balance.

Personally, I feel that iodine may be tried with impunity in exophthalmic goiter, if results are carefully noted. Most cases of untoward effects seen are due to the *abuse* of iodine through lack of proper observation. Large doses are, of course, dangerous in nearly all cases of exophthalmic goiter and should be avoided, excepting where the disease seems to be of syphilitic origin, in which instances rapid improvement is seen. However, we meet with exceptional cases of exophthalmic goiter without evidences of syphilis in which small doses proving harmless, the dosage is cautiously increased and the patient is finally cured. I was bold enough to administer gradually increasing doses of potassium iodide in a very severe case of Graves' disease some years ago, and the patient is alive and well today. The dose was 5 gr. three times a day, increasing the dose by 1 gr. daily. There being a tolerance to the drug and manifest improvement, it was continued until the patient was taking 1 dr. of the iodide three times daily. Catarrh of the larynx caused me to discontinue the drug for two weeks, when I again prescribed 5 gr. thrice daily, increasing the dose as before to 1 dr. The goiter gradually disappeared, and the exophthalmos, tachycardia, tremor, and other symptoms were greatly ameliorated in a few weeks. Within six months he gained 20 pounds, and within fourteen months he was discharged cured. There were no evidences of syphilis. In addition to this treatment, local iodine medication, with the usual dietetic and hygienic measures, was adopted. I have since obtained similar results from iodine therapy in Graves' disease, more especially from the local application of iodine combinations. It has been suggested that the salutary effects of iodine in this disease are probably due to a partial influence on the enlarged thymus gland—a tissue which yields readily to iodine therapy. However that may be, it remains for future study to fathom the depths of the pro and con of this question; meanwhile we may employ iodine in cases of exophthalmic goiter if we deem it wise, but it must be used with caution.

Intestinal Antiseptics.—These are advocated by McCarrison as efficacious in the treatment of exophthalmic goiter in cases which appear to be of intestinal origin. He advises *thymol* in 10 gr. doses or more, night and morning, administered in the form of a coarse powder which is washed down with a draught of water. The bowels are kept active by a suitable laxative, and all solvents of thymol are excluded from the dietary.

Sodium phosphate has been employed by Vetlesen in a series of 40 cases, all being benefited in varying degree. This substance is said by some to possess properties antagonistic to the toxemia of Graves' disease. Whether or no this is true, its administration in doses of 1 dr. in a tumblerful of hot water every morning enhances the possibilities of recovery by its favorable influence on the liver and bowels, stimulating the emunctories to full physiologic function.

Sodium salicylate in 10 gr. doses four times a day has resulted in benefit in the hands of a few observers. Dr. J. M. Anders reports a few cases in which there was almost total relief by the use of sodium salicylate. *Sodium glycerophosphate* was found to reduce the size of enlarged thyroid glands by Trachewsky in Kochers' clinic. Starr also has found this remedy of great service in several cases.

Oil Injections.—Oil injections into the bowel are suggested by Ebstein as essential in every case of exophthalmic goiter, in order to remove all impacted feces which may be the cause of constipation or diarrhea. This author reports four cures by this method.

Dechlorination.—Dechlorination is advocated by K. Alt. He employed this treatment in 12 cases of Basedow's disease and claims to have obtained complete cures within a few months by his method. The patients were gradually restricted to a maximum of 4 gm. of sodium chloride with food daily; liquids were also restricted. Hydrocarbons were given only in amounts tolerated, but the diet was made as nourishing as possible through a maximum of proteids and fat, much whipped cream and fresh butter being insisted upon. Dechlorination was enhanced by the drinking of carbonated waters. According to Dr. Alt, a woman of fifty-four who had lost weight until she weighed 34 kilos, and whose mental condition was such that she frequently attempted suicide, was completely cured after two months of treatment.

Calcium salts, especially the lactate, are to be tried in unusual cases not responding readily to quinine therapy. Blair Bell, Sir John Barr and others have shown that calcium exerts a powerful influence on thyroid metabolism. I usually combine the calcium lactate with suprarenal and parathyroid gland, with good effect. Incidentally, I would especially recommend the prolonged administration of calcium during pregnancy in subjects of exophthalmic goiter, in order to lessen the prospects of prepartum or postpartum hemorrhage.

Belladonna and **atropine** if employed, must be carefully guarded, as they depress the vagus and are apt to increase the tachycardia. Where the hyperidrosis is a troublesome factor or where polyuria is excessive, the extract of belladonna, alone or combined with other suitable drugs, should be given cautiously and only until the indications for which it is given are overcome. Belladonna, in some instances, seems favorably to influence the nervous symptoms and the action of the bowels.

Digitalis and other cardiac stimulants should never be employed excepting where strongly indicated by a dangerous lagging of the tonus of the circulatory system. Where the heart is losing compensation and enlarging to an alarming degree, and the blood pressure is far below normal and the ankles are becoming swollen, digitalis is *not* the drug of choice, but *strophanthus* or *spartein sulphate* should be employed. The same objection may be voiced against ergot, but ergotin seems to be well tolerated. In the presence of the above indications pituitrin should also be tried. Strophanthus is, generally speaking, the cardiac stimulant of choice and may be given in doses of gtt. x to xv, three or four times a day. *Nux vomica* and *strychnine* are rarely, if ever, to be employed. In some instances of impending cardiac failure, especially where a degree of plethora exists and the diastolic pressure is high, careful venesection may be tried with a view to relieving the right heart and the congestion of the lungs, liver, and other organs. It may be necessary to repeat this procedure several times until circulatory tonus is reestablished.

Nerve Sedatives.—Nerve sedatives certainly occupy an important position in the treatment of a condition so marked by nervous manifestations as Graves' disease. The *bromides* are the most important of this class of remedies, the favorites being the sodium and strontium salts. The tremor, tachycardia, and insomnia are benefited, and the patient soon evinces a feeling of well-being under careful bromide therapy. *Veronal* has its advantages, in that the bromide rash is avoided, and is in most respects equal to the latter drug in therapeutic effects. Two or 3 gr. of veronal thrice daily is the dose equivalent approximately to 15 gr. of sodium bromide three times a day. *Sulphonal* and *trional* have their advocates. *Hyoscine hydrobromide* in gr. 1/250 doses twice daily, has been used successfully in efforts to control the nervous symptoms of exophthalmic goiter. Where insomnia and nocturnal polyuria are troublesome, this drug is quite valuable. Except during an attack of hysteria or insanity, opium and its derivatives should never be used in exophthalmic goiter as nerve sedatives. By far the best nerve sedative in this condition is, in my experience, veronal, as a substance which is not only devoid of the habit-forming property, but after a restful night's sleep, the patient is calmer and more tranquil during the following day.

Ichthyol.—Ichthyol has in my experience proved of brilliant service in exophthalmic goiter. How it exerts its beneficent effects I am unable to conclude, but the results obtained are somewhat similar to those of the quinine salts. It is a very efficient alterative, improving appetite and digestion, and is a better means of instigating an increase in weight and sense of well-being than any drug in the materia medica. In combination with quinine it becomes a very powerful formula, controlling the cardinal symptoms more promptly than anything I have ever used. At times patients rebel against taking ichthyol, because it "repeats" on them with a sort of nauseating odor and taste, but this objection soon disappears, and a tolerance is acquired.

Having discussed the afore-mentioned remedial agents in a more or less isolated manner, I submit the following formulæ to the reader as combinations which have yielded excellent results in the treatment of exophthalmic goiter. In presenting these prescriptions, I do so with the understanding that they are intended for the *average* case of Graves' disease; but the presence of an *unusual* symptom or the *intensification* of a *usual* phenomenon may require modifications or the introduction of other drugs, at the discretion of the physician in charge.

Formula 1:

℞	Quinin. Hydrobrom.	gr. v
	Ergotin	gr. i
	in capsule 3 or 4 times a day.	

This is the Forcheimer treatment which has yielded him 82 per cent of cures in 71 cases. J. M. Jackson and L. G. Mead in the out-patient department of the Massachusetts General Hospital have treated 85 patients in this fashion with 76 per cent of cures. The ergotin may be omitted, or, it may be discontinued some weeks or months after treatment is begun. The quinine must be continued for at least one year after all evidences of the disease have disappeared.

Formula 2:

℞	Quinin. Hydrobrom.	gr. v
	Ergotin	gr. i
	Arseni trioxidi	gr. 1/40

in capsule 3 or 4 times a day.

Formula 3:

℞	Quinin. Hydrobrom.	gr. v
	Ergotin	gr. i
	Ferri Arsenias	gr. 1/12

in capsule 3 or 4 times a day.

Formula 4:

℞	Quinin. Hydrobrom.	gr. v
	Ergotin	gr. i
	Arseni trioxidi	gr. 1/40
	Massa ferri carb.	gr. ii

in capsule after meals and at bed time.

These formulæ (2, 3 and 4) are intended especially for subjects of exophthalmic goiter with an evident degree of secondary anemia. The same class of patients might be given ichthyol in addition as follows:

Formula 5:

℞	Quinin. Hydrobrom.	gr. v
	Arseni trioxidi	gr. 1/40
	vel Ferri arsenias	gr. 1/10
	Ichthyoli	gr. i

in capsule after meals and at bed time.

The ichthyol may be increased to gr. ii or iii as the tolerance for it increases. This prescription may be combined with a digestive ferment as follows:

Formula 6:

℞	Quinin. Hydrobrom.	gr. v
	Pancreatin *vel* Taka diastase	gr. iv
	Ichthyoli	gr. i
	Arseni trioxidi	gr. 1/40

in capsule 1/2 hour after meals.

In the presence of apparent adrenal insufficiency and where the arterial tonus is exceptionally poor, or even on general empirical grounds, the extract of suprarenal gland may be combined as follows:

Formula 7:

℞	Quinin. Hydrobrom.	gr. v
	Ext. Glandulæ Suprarenalis	gr. ii
	Arseni trioxidi	gr. 1/30

in capsule 3 or 4 times a day. Or,

Formula 8:

℞	Quinin. Hydrobrom.	gr. v
	Ext. Glandulæ Suprarenalis	gr. ii
	Spartein. Sulph.	gr. 1/4
	Arseni trioxidi	gr. 1/30

in capsule 3 or 4 times a day.

The following is a very excellent combination in exceptionally marked asthenia:

Formula 9:

℞	Quinin. Hydrobrom.	gr. iv
	Lecithin	gr. i
	Ext. Glandulæ suprarenalis	gr. iss
	Arseni trioxidi	gr. 1/30
	Pancreatin	gr. iv

in capsule 1/2 hour after meals and at bed tin

By far the most useful formulæ are those contai onal, as the insomnia, restlessness, and nervous ity are very soon overcome:

Formula 10:

℞	Quinin. Hydrobrom.	gr. v
	Veronal	gr. ii
	Ferri Arsenias	gr. 1/10

in capsule 3 or 4 times a day.

It will be found that after the above formula is tered for a month or two the nervous symptoms v nearly in complete abeyance that the veronal ma creased to gr. i to each capsule, or altogether omitt

Cases of extreme hyperidrosis will yield to the f

Formula 11:

℞	Quinin. Hydrobrom.	gr. v
	Ext. Belladonnae	gr. 1/4
	Veronal	gr. ii

in capsule 3 or 4 times a day.

The belladonna may be discontinued when the skin excess of moisture. In some cases I have found sary to include it intermittently until the complete cure of the syndrome was effected.

Finally, when confronted by a new case of exophthalmic goiter which is approximately of 12 to 18 months' duration, the symptomatology appearing typical, I write for the following:

Formula 12:

℞	Quinin. Hydrobrom.	gr. v
	Arseni trioxidi	gr. 1/40
	Lecithin	
	Veronal a. a.	gr. ii
	in capsule 3 times a day.	

Instead of lecithin, ichthyol may be used.

It is seen from the above formulæ that quinine hydrobromide is a constant ingredient in the successful treatment of exophthalmic goiter. This is so because of its harmlessness on the one hand, and its almost specific effect on the hyperplastic thyroid, on the other. These formulæ may be changed *ad libitum,* depending upon individual indications, but we must always include the quinine if we are to be assured of success.

V. Local Treatment

The local treatment of exophthalmic goiter, *i.e.,* treatment directed to local areas, especially the thyroid, may supplement the various other measures in treatment. Local treatment, although not dependable if employed alone, and perhaps not *essential* to success in the majority of cases, seems to act synergistically with all other efforts directed toward the general good of the patient, either through actual local effect, a psychologic influence, or both. I have successfully treated cases of exophthalmic goiter *without* local measures, and have not regretted it; on the other hand, if the thyroid gland is rather large, I combine general with local treatment and feel convinced that the combination hastens recovery.

Local treatment may be divided into (*A*) medicinal; (*B*) miscellaneous.

(A) Medicinal

In spite of apparent contraindications, the iodine preparations seem to yield benefit or at least are harmless in the local treatment of exophthalmic goiter, if combined with other measures antagonistic to thyroid hyperactivity. The tincture of iodine *is* contraindicated, not because of the iodine content, but because of the irritation which, after the second or third application, causes the skin to become parchment-like and unable to absorb medicaments. Moreover, the discomfort and pain, the discoloration of the skin and consequent embarrassment, and the possibility of a troublesome eczema, are apt to increase the nervousness of the patient. The so-called colorless tincture of iodine does not discolor the skin, nor does it posses any therapeutic virtues in these cases. The ideal treatment is the use of weak iodine solution or of nonirritating ointments containing iodine or one of its salts.

It seems that the quantity of iodine actually absorbed into the system through application over the thyroid area is negligible and incapable of any apparent systemic effect. At the same time, the mild counterirritation and the quantity of local absorption appear directly beneficial. And so, as we go on from case to case in which patients have been restored to complete health, we can not help but be impressed with the tangible benefits derived from these local treatments, and since "the proof of the pudding is in the eating" and the patient is not interested in theories but wants relief, we must set aside the theoretic objections to iodides so far as these local applications are concerned. The practical method in a matter of this sort, at least for the present, is to follow the precepts of the empirical deduction that not only are these medicaments harmless, but seem of decided benefit in a certain percentage of cases. As before mentioned, these applications are to be tried as supplementary measures in all cases where the thyroid is unduly large, and are to be continued for two or three months, or until the thyroid has been reduced to normal or nearly normal, when they may be discontinued.

I would recommend the following formulæ:

℞ Mentholis gr. ii
Camphoræ gr. v
Tr. Belladonnæ ℥ ss
Tr. Iodini q. s. ad. ℥ i
Misce.
Sig.: Paint lightly over the thyroid area at bed time daily or bidaily.

As the above formula slightly discolors the skin, the patient may be given the following:

℞ Ungt. Potassii Iodidi ℥ ii
Sig.: Use at bedtime.

A small portion the size of a lima bean to be rubbed gently over the goiter area until absorbed, after which a small quantity is to be lightly smeared over the thyroid area, and a soft cloth is to be placed about the neck and kept on all night. In applying the cloth about the neck on retiring, moderate pressure may be used, the cloth of course to be fastened posteriorly. I have observed that the nocturnal repetition of this moderate pressure has served in some instances to cause a more rapid diminution in the size of the thyroid gland. The pressure should not be great enough to give rise to discomfort or to disturb sleep, but should be somewhat similar to that experienced when wearing a tight collar about the neck. In some cases, the skin is exceedingly tender and will become rather hyperemic after the application of the above ointment. In such instances, the patient should be instructed to dilute the small quantity of ointment used each night with a sufficient quantity of cold cream.

The following combination is also very serviceable:

℞ Ungt. Hydrarg. oxidi Rubri ʒ ss
Ungt. Potassii Iodidi
Lanolini a. a. ℥ i
Misce.
Sig.: As in preceding formula.

(B) Miscellaneous

Under this classification is included suggestions offered from time to time for the local treatment of exophthalmic goiter, and for which certain degrees of success are claimed.

An *ice cap* applied over the thyroid in rapidly developing hyperplasia is very beneficial subjectively and objectively. In markedly vascular goiters, especially where the throbbing is troublesome, this procedure is as grateful to the patient as an ice cap applied to a turbulent heart. Incidentally, a throbbing thyroid is usually caused by a palpitating heart, and an ice cap over the heart and another over the thyroid at the same time assist materially in favorably influencing the patient's comfort.

Sand or salt bags, weighing about 2 pounds, placed over the goiter while the patient is in the recumbent position, have been tried by E. Mingus with asserted success. This observer reports 3 cases in which this measure proved highly valuable. In one case the gland was so reduced in size that in two weeks it was hardly noticeable, the heart quieted down, and the tremor disappeared. I find that patients do not readily cooperate with this treatment, stating that when they fall asleep the sand bag falls off the neck, or if it is fastened on, a change in position during sleep changes the center of gravity of the weight and the pressure is removed.

Adhesive plaster applied about the neck (zinc, belladonna, or adhesive) seems a reasonable procedure. Mild persistent pressure by this means (unless pressure symptoms already exist) can do no harm, and may assist other measures in lessening the size of the goiter more quickly in a given length of time. Patients do not rebel against this treatment if the plaster material is properly applied.

Flexible collodion has also been employed for the same purpose as plaster, but has no advantages over the latter. In most instances it will be found that plaster is more agreeable to the patient.

Injections of various substances into the thyroid gland have been practiced for many years, and though many successes are claimed for this method of treatment, it has fallen into general disrepute in the treatment of exophthalmic goiter. Such substances as tincture of iodine, chromic acid, iodoform, osmic acid, and other chemicals have been advocated from time to time. The purpose of injections is to reduce the size of the gland by the formation of areas of sclerosis. These substances are injected directly into the parenchyma of the gland, the needle being first employed to aspirate in order to determine whether a vein is reached. Injections are made as often as the exigencies of the case in hand require.

Joseph E. Sheehan reports a series of 17 cases which he treated with injections of *carbolic acid, iodine* and *glycerine.* Five drops of equal parts of carbolic acid, C. P., tincture of iodine and glycerine are injected into the most prominent part of the goiter, usually at five day intervals. In many of the cases, five injections suffice, particularly in the ordinary enlargement which occurs in young women where there is no evidence of toxin absorption. Sheehan states that if five injections do not suffice, many more can be given with perfect safety. The asserted beneficial effect of this treatment, he claims, is due to a sclerosis of the gland, thereby modifying the abnormal function of the organ, alleviating pressure symptoms. At first, an inflammatory reaction occurs in the gland, followed by cicatricial adhesions and consequent obliteration of the cells. Glycerine is used as a solvent. After the injection the patient complains of pain and swelling, the pain of which terminates into soreness in twenty-four hours. If the swelling and pain continue, codeine in small doses with ice applied over the goiter will give prompt relief. Of the 17 cases treated in this manner, 15 were of the nontoxic type, a few of which possessed an associated glycosuria. Fourteen of these cases were almost, if not entirely, cured. Two of Sheehan's cases were toxic in type and seemed to respond very favorably to the treatment. Sheehan suggests that this treatment should be combined with a course of arsenic medication and with some form of the phosphates.

Quinine and Urea Injections.—Watson has employed this method extensively. He recommends it only to relieve hyperthyroidism and not to remove the goiter. Although he claims that a small toxic or atoxic goiter may, through the reaction, disappear, the process is slow, usually covering several months, and when used for this purpose alone, the results are liable to be disappointing. The injection must be employed with discretion and is suitable for use only in a hospital by men skilled in goiter work, as an inexperienced operator is liable to inject too deeply or to make the injection within the trachea. Watson further states that the indiscriminate use of quinine and urea, in the hands of one not familiar with the low threshold of stimuli possessed by the average case of toxic goiter, is liable to produce alarming symptoms of hyperthyroidism which might result disastrously. He obtains the best results by keeping the patient in bed in a hospital for several weeks while giving the injections, the length of time depending on the severity of the symptoms and response to treatment. It is absolutely necessary to employ a local anesthetic at the site of injection. In order to prevent an acute attack of hyperthyroidism, the patient's threshold to stimuli is raised by means of preliminary injections at one to three days' intervals, of a few minims of sterile salt solution followed by injections of sterile water, into the most prominent part of the thyroid. After two to four preliminary injections, the nervous reaction is so diminished that the quinine and urea can be given with only slight discomfort and no increase in symptoms; as soon as there is no hyperthyroidal reaction following the water injections, their usefulness is at an end. The quinine and urea injections are made into different parts of the tissue each time. An all-glass syringe of 1 to 2 c.c. capacity is used, and after the usual aseptic precautions, the tissues down to the gland are anesthetized with a weak cocaine or novocaine solution. The syringe is now detached and the needle is thrust carefully into the body of the goiter. After ascertaining that there is no fluid in the thyroid and that no blood or air comes through the needle, the syringe is attached and the infiltration slowly made. In cases of hyperthyroidism, from 1 to 4 c.c. of a 30 to 50 per cent quinine and urea solution are administered at a treatment, repeating the injections about every third day, depending on the progress of the case. Watson administers eight to fifteen infiltrations, accomplishing thereby a marked improvement in the general symptoms and the disappearance of the bruit over the superior thyroid arteries. He concludes from his observation that the method is to be employed only in efforts to control the symptoms of hyperthyroidism and is not to be recommended as a means of causing the disappearance of the tumor. He suggests that the injections will not relieve the symptoms of advanced toxic goiter where the vascular and nervous systems have been permanently damaged. He further believes that the greatest field of usefulness for this injection will be found in those cases of beginning hyperthyroidism not severe enough to justify operative treatment, and as a preparatory measure to partial thyroidectomy in chronic cases of toxic goiter in which the patient is too ill to warrant any form of immediate operative procedure.

Boiling water injections were introduced by Miles F. Porter whose technic is as follows: The skin and the area to be injected are thoroughly anesthetized by the injection of a free quantity of ½ of 1 per cent novocaine solution. One of Porter's steel syringes, taken out of the boiling cauldron, is filled with boiling water, which is immediately injected by inserting the needle well into the substance of the mass. To prevent scalding, the skin and the contiguous surfaces are shielded by a covering of towels, leaving only the point of injection exposed. As the steam or water is apt to escape from the needle as it approaches the skin, a gauze swab is held as a shield in front of the needle, which latter is thrust through and into the skin, when the contact is made. From 10 to 20 minims are forced out in one spot. The needle is then partially withdrawn, and the point carried to a new field, and the injection repeated. Three or four such areas may be injected at one sitting, and these may be repeated as required, in one or two weeks, and so on, until the tumor disappears. A Bunsen burner or an alcohol lamp held under the barrel of the syringe just as the needle is being inserted, will insure a high temperature. It is advisable not to have the point of the needle immediately under the skin, as the excessive heat so directly applied, may produce necrosis, which is apt to become a point of infection. If the skin covering remains intact, all tissue coagulation or destruction, being aseptic, is harmless, and the solidified mass gradually disappears by granular metamorphosis. Important vessels and nerves, as well as the trachea, should be avoided.

In commenting upon this treatment, James W. Markoe states: "The use of quinine and urea is similar to the use of boiling water employed by Charles Mayo and others, and to the use of phenol and boiling water employed by Ochsner. The result of these injections is a marked edema in the tissues, sometimes with fatal issue. I think this result has occurred in 1 or 2 cases. Although Dr. Watson has reported some splendid results, I think we must sound a note of warning not to inject any of these substances at random. We may have complication of acute edema with sudden death."

A. Caballos and G. Bacigalupo report the results of treatment of six patients by the Porter method. Two of the patients were men and the remainder women. As many as thirty injections were administered. Some of their patients were observed for two years, the others for one year following the treatment. They noted a decrease in the size of the thyroid. In three patients, after two years of treatment, the pulse rate diminished from 130 to 100 beats per minute. The exophthalmos was unaltered. The subjective symptoms were decreased by the treatment, and the patients felt better.

Charles H. Mayo (Abstract of Discussion, Journal A. M. A., September 14, 1918) states that he has had three patients die from the injections of boiling water. "They were treated in their beds to prevent shock, the water was probably not hot enough to coagulate albumin, and possibly more easily enabled the gland to throw off the hormones of secretion."

It can readily be seen that the injection treatment in true hyperplastic goiters is neither reliable nor safe. This mode of procedure may be very efficacious in nontoxic goiter, but in the vascular goiter of Graves' disease many things may happen in consequence, among which are hemorrhage, infection, dangerous dyspnea and sudden death from the injection of the substances into a blood vessel.

VI. Electrotherapy

Here we enter a domain but little understood, simply because we are still ignorant of the nature of electricity itself. We *do* know, however, that the effects of electricity in certain forms in certain cases seem favorable, and it is this assumption that lends popularity to electrotherapy in exophthalmic goiter. It can not be denied that the beneficial effects observed in some cases are in part due to mental suggestion, but when we see other cases not very susceptible to mental influences improve, we must conclude that a certain percentage of cases is benefited by this mode of treatment. And here again we must qualify our statements by saying that electricity *alone* helps only in rare instances. Electricity must be employed as a supplement, not as a mainstay; it must be combined with the necessary hygienic, dietetic, medicinal and other measures, if we would have it serve at all. In fact, the same may be said of any other single remedial measure herein mentioned—each must be combined with all the rest in order that prompt recovery be achieved. The quinine treatment is, however, an exception to this rule. A marked case of exophthalmic goiter may be successfully treated by a definite formula containing quinine as before outlined, without the assistance of other means and measures. But in order to obtain a maximum of good results, the Basedowian process must be attacked from every possible avenue.

X-Ray Treatment.—X-ray treatment has become quite popular in recent years. It is based on the property of glandular inhibition, observed when living tissue is exposed to the rays. Following inhibition of function, the continuation of effects leads to cellular alteration with final necrosis, to such an extent that occasionally a Basedowian state of the patient is converted into one of myxedema. On the contrary, an instance is occasionally met with in which an increased glandular stimulation was the result, with intensification of the symptom. Let us examine the opinions of a few clinicians on this subject, gleaned from recent literature.

According to Lédoux-Lébard, in cases benefited by x-ray the symptoms are improved in the following order: disappearance of nervous phenomena, improvement in general well-being, return to the normal or to near normal of the cardiac frequency, and finally diminution in size of the thyroid and improvement in the exophthalmos. According to Hernaman-Johnson, x-ray treatment is highly efficient in the therapeusis of exophthalmic goiter, the best results being obtained when the application is made at frequent intervals—not less than three times a week in mild cases, in acute cases, daily. Hard rays, filtered through aluminum should be used. Causes of failure are pain, anxiety, fatigue, constipation and dental trouble.

Of the 80 cases under treatment at the Massachusettes General Hospital, M. Seymour reports all improved except 7. Five of these showed no change. Of the 80 cases, 8 were completely cured of their symptoms. They use a dose of 4H (equals 4 Holzknecht, or 10x Kienbock, or 1B Sabouraud-Noir). This produces a slight erythema, but no skin irritation. The target is 10 inches from the skin with a filter of 4 mm. of aluminum, and one thickness of sole leather. The dose is not repeated within three or four weeks. Seymour also finds the evaluation of the basal metabolism of distinct value as an index of thyroid activity. Five cases of extra-cervical ribs were found in the 144 cases studied, but no symptoms could be traced to this abnormality.

S. Nordentoft (quoted in Endocrinology, Vol. II, No. 4) reports 50 cases of exophthalmic goiter given roentgen treatment, and discusses the participation of the thymus. The roentgen exposure was made for from forty to sixty minutes, at one sitting. Two or three exposures generally sufficed with intervals of from four to six or eight weeks. The subjective treatment was marked from the start, the restlessness, tremor and subjective heart disturbances subsiding first, the goiter and exophthalmos more gradually, the tachycardia last of all. Even in the most favorable cases, the patients still display an unstable pulse and tendency to tachycardia on slight provocation. In several cases the desired effect was realized with a single exposure. This method of a few large doses with long intervals may prove to be better adapted for certain cases than for others. In any event, it is far more convenient for all concerned than a large number of smaller doses. His 50 patients were given a total of ninety-nine sittings; in eighty-four the thymus was exposed as well as the thyroid, as he is convinced that the thymus is a factor in certain cases of exophthalmic goiter.

Pfahler and Zulick believe that the x-ray has a field of distinct usefulness in the treatment of this form of goiter. A preliminary roentgenogram of the chest should be made in all cases in order to obtain some information as to thymic size and as to substernal extension of the goiter. When the thymus is not found enlarged, a single dose directed through the sternum will be sufficient. When it is enlarged, the rays should be passed through two fields on either side of the median line below the clavicles, including the first, second and third spaces. The dosage must be carefully regulated so that the total amount given the patient is known. The series decided upon should not be repeated inside of three or four weeks. Sometimes it is advisable to divide the treatment so as to give a dose through only one or two fields at a time. After there is a distinct improvement in the symptoms, the interval should be prolonged, for there is danger of reducing the secretion of the gland to the extent of producing the symptoms of hypothyroidism.

Walter, of the Johns Hopkins University, treated 60 cases of exophthalmic goiter with the roentgen rays. In each case treatment was directed toward the thymus gland through areas 5 cm. in diameter, in the first second and third interspaces on both sides of the sternum. Treatments were given in three series, 6 doses to each series, each dose amounting to 7 1-2 H. Sixteen patients received the full three series of 134 H., of which 50 per cent were apparently cured. Seven showed marked improvement, and one failed to respond to treatment. Of 9 patients who received two series, 2 were cured, 5 showed improvement, and 1 did not improve. Twenty-four patients have received one series of treatments, and some of these showed improvement. The first evidences of improvement are seen in the amelioration of the nervous symptoms and the improvement in the general health. Soon afterward there is a retardation of pulse rate and an improvement in the blood picture.

Dr. Florence Stoney, in a series of 48 cases of Graves' disease treated with x-ray, reports 14 cures, 22 cases sufficiently improved to return to the duties of life, 4 who were unimproved, 7 who discontinued treatment too soon to form an opinion regarding the efficacy of the treatment, and 1 in whom the pulse rate fell from 136 to 112 and who died twelve hours after operation. She gave 6 milliamperes 5 minutes at a focal distance of 6 inches, treating each lobe separately. Treatments were given twice a week for a month; at times a slight dermatitis was produced. An interval of two weeks was allowed between a month's series of treatments, and the total length of time of treatment was from six to eight months.

Simpson (Medical Record, September 4, 1915) reaches conclusions as follows as to the use of the x-rays in Graves' disease:

1. Many cases of exophthalmic goiter are associated with enlarged thymus glands, and this association often causes serious postoperative symptoms and even death.
2. While such an association will seriously complicate and prolong a surgical operation, it offers no such added difficulties for the roentgen therapeutist.
3. Not only such ductless glands as the ovaries and testicles, but also the enlarged thyroid and thymus glands, as well, are very sensitive and may be atrophied by the roentgen ray.
4. This theory has been amply proved by laboratory experiments and clinical results in many cases of hyperactivity of the thymus gland seen in cases of status lymphaticus and hyperactivity of the thyroid gland—exophthalmic goiter.
5. If these cases of status lymphaticus and exophthalmic goiter will give the roentgen ray a fair and impartial trial, the majority of them will be relieved of all troublesome symptoms and make unnecessary a disfiguring, dangerous and often futile operation.

Sielmann has given 21 Basedow patients systematic roentgen treatment in the last five years. The total duration of treatment was from six weeks to six months, and he never allowed the exposure to reach the point of inducing a dermatitis. One patient, who was a young man with palpitation for a period of eight years, developing into pronounced typical Basedow's disease was remarkably improved by four exposures, and by the end of three months, interspersed with three weeks' pauses, he was practically cured. The neck was 4 cm. smaller in circumference and the pulse, formerly 120 or 160, was permanently 80 and the exophthalmos and tremor had entirely disappeared. Another case teaches that an operation on the thyroid always a complete cure. The improvement for after the roentgen yielded to a stormy recu syndrome, and operative treatment was applie followed by apparently a complete cure for a y the whole syndrome returned again, but was b by a few roentgen exposures. Another less case is that the ovaries, the pituitary body and evidently cooperate in bringing on Basedow's thyroidectomy does not remove all the cause

Russell Boggs believes that the roentgen trea a good prospect of cure without operation in centage of cases of exophthalmic goiter. T treatment should be directed to the thyroid, cases the thymus should also be rayed; this is and should not be attempted by any one unfami technic and the physiology of the ductless gland symptoms of improvement are a decrease in th and an increase in weight; the reduction in th thyroid is not always marked even after the di of all symptoms, and the exophthalmos is the improvement. Even if operation is found to b later, the mortality will be lessened by a prelim treatment, the aim of such treatment being sufficient atrophy of the thyroid so that it will a normal amount of secretion and no more.

G. W. Gries does not believe it advisable to roentgen ray treatment of exophthalmic goiter. sive dose method of treatment is especially dang acute type. The first improvement noted is in t ness and the pulse rate. This is followed by in the weight and an improvement in the other Formerly gas tubes were used; now the Cooli used. The mild cases of hyperthyroidism may medically and by the roentgen rays. In acute mic goiter roentgen treatment is the most satisf chronic exophthalmic goiter the choice lies equal roentgenization and operation. The roentgen treatment is slower, but there is not so much danger in producing a subsequent hyperthyroidism as by operation. The death rate from x-ray treatment is nil. Where hyperthyroidism develops in an old goiter roentgen treatment is only palliative.

Freund reports having obtained good results in 5 cases treated by the rays. In all of his cases there was a reduction in the size of the thyroid and coincident with this reduction in size, there was a diminution in the severity of the other symptoms, the previous symptoms subsiding, the heart beating more slowly and the patients increasing in weight. One of his patients, a young woman, had been ill six months before coming for treatment. She was under medical treatment for two months, but there was no improvement. She was given two treatments with an interval of one week between exposures. After this she improved rapidly, the goiter disappeared, and no tremor or recurrence could be detected. Freund thinks that the roentgen rays meet the indication for treatment by restoring normal conditions to a hypersecreting thyroid gland.

Hirschl reports that x-ray treatments of Graves' disease result in an increase in body weight, lessened tachycardia, improved mentality, and cause a disappearance of the glycosuria. Tremors, hyperidrosis and exophthalmos are improved.

Faber, in 8 cases treated by roentgen therapy, obtained striking results in part of the series. One patient,—a married woman who had symptoms for four years, was given seven treatments of ten minutes each in the course of twelve days, and the treatment repeated a month later. Four months after the second series of treatments, she wrote that she was well.

S. Stern of New York states that he has treated about 250 cases of exophthalmic goiter in the past seventeen years. The cases of cystic goiter were ruled out as they did not respond to radiotherapy. They were referred to the sur-

geon. In regard to radio effects,—small doses wer
lating; large doses inhibitory in effect. Very lar
caused atrophy. The question was entirely one of
It had to be very carefully regulated to accomp
the result required on the cells of the gland. T
ment was getting easier year by year as knowled
diation increased. The point would be reached
cases of Graves' disease or exophthalmic goiter
operated upon. With medical treatment and radi
lief could be given in all cases. The first symptom
to radiation was nervousness and insomnia; the ne
cardia (although it was difficult to get the exact p
as the patient was usually excited by coming to
sician's office). The pulse rate should be taken
The size of the thyroid would be reduced in the
of cases. In some it did not diminish entirely.
ophthalmos was the most difficult symptom to ch
the last to disappear, but within the past two yea
nic by means of defiltered rays seemed to accomp
results in regard to this symptom. The last ten w
given better results, and in 4 cases this sympto
tirely disappeared.

Regarding the dosage of x-ray treatment, Pfa
"Generally speaking, with a Coolidge tube, tr
current, a parallel spark gap of 9 inches, and the
the tube 8 inches from the skin, 5 milliamperes o
given for five minutes through 3 mm. of aluminu
layer of sole leather, will give 18 to 20-x or appr
double tint 'B,' and this is the dose we generally

Secher reiterates that the enlarged thyroid gland
to roentgen treatment in very different ways in
cases. In several cases cited, an ordinary goiter
become transformed into the exophthalmic ty
roentgen treatment. Belot and Simon, among ot
declared that a correctly given course of roent
ment is free from danger, but Secher insists that
true. The thyroid may be whipped up to function

or it may become functionally insufficient. A tendency to myxedema, however, is rare, but numerous cases of aggravation of hyperthyroidism have been reported, even with the most modern improved technic. Rieder and Verning have each reported 1 or 2 cases in which the aggravation was so intense that the patient died, and Secher now adds another case to this list of fatalities. His patient was an unmarried woman of forty, previously healthy until exophthalmic goiter developed. The thyroid was given roentgen treatment after a year, eight exposures, each 1-2 Saubouraud Noiré unit distributed in four fields, three on the thyroid and one on the thymus. Her symptoms became much aggravated at once, with restlessness, choreiform movements, pulse 100 to 200, and heart beat up to 240, respiration 72, and death the fifth day. The thyroid showed very slight changes and the thymus nothing abnormal.

According to most authors, the subsidence of every symptom is rare under treatment by x-rays, but improvement is claimed in approximately 50 per cent of cases. In concluding this brief review of x-ray treatment in exophthalmic goiter, it must be remarked that one can not accept any opinion on the subject as conclusive. Roentgen treatment attacks the thyroid gland *alone* as does thyroidectomy, and is open to the same objections as the latter, excepting that there is little or no mortality or operative complications. To try x-ray treatment *alone* therefore, is almost harmless, excepting that the delay in instituting the proper successful nonsurgical measures may mean a delay in convalescence. On the other hand, x-ray treatment may *supplement* the other measures herein emphasized, with advantage, just as was stated in speaking of local applications to the neck.

Radium.—Aikens, of Toronto, reports several cases of exophthalmic goiter in which radium, combined with approved nonsurgical measures, yielded satisfactory results. Of course, the satisfactory outcome can not be proved as resulting from radium alone, and I am inclined to believe that the other dietetic, hygienic and medicinal measures employed were really the curative agents. Victor Horsley and Finzi state that the most constant changes wrought by radium in this disease are observed in the blood and lymphatics.

Dawson Turner believes that radium has two definite advantages over x-rays in the treatment of exophthalmic goiter—namely (*a*) it can be given in definite doses, and (*b*) it can be applied without noise or excitement while the patient is in bed.

Galvanism.—Oliver reports 2 cases in which the ultimate results of treatment by galvanic electricity proved highly gratifying. The first case was that of a woman of twenty-six years, suffering from the disease for three years, in whom hematothyroidin had failed and section of the cervical sympathetic had been refused by the surgeon, owing to the patient's extreme weakness. Her weight had become reduced to 37 kilograms. A sixty volt galvanic current was subsequently employed, with broad electrodes over the neck and back, the former being negative and the latter positive. The amount of current was gradually increased to 80 milliamperes. Thirty-seven treatments in all were administered, at first daily, later at increasing intervals, up to one week. Each sitting lasted about half an hour. Five months after the beginning of treatment, the patient weighed 59 kilograms and her pulse rate had fallen from 140 or 150 to 80. The second patient was a woman of forty-eight years, with extreme tremor preventing locomotion, a pulse rate of 180, a large soft goiter, diarrhea, vomiting, and marked emaciation. Forty-two galvanic treatments were given. After the eighth treatment the patient could already walk a considerable distance. When seen three years later she was in good health. This author deems the galvanic current one of the best procedures in exophthalmic goiter. The ordinary dose of 25 to 35 milliamperes is, however, insufficient, even if combined with faradic electricity; a much stronger treatment is required.

Schvostek (quoted by Forcheimer) employs the galvanic current as follows: (1) To the sympathetic nerve: anode to sternal notch, cathode to the angle of the jaw for one minute; (2) to the spinal cord: anode over fifth dorsal vertebra, cathode on the neck; (3) through both mastoid processes: weak currents and daily sittings. Says Forcheimer: "There are many modifications of this method; all seem to be directed to galvanization of the soft parts of the neck; indeed, this seems true of the application of electricity in any form. There is no doubt of the efficacy of electricity in this disease; many cases have been cured and more have been improved. But there are more refractory cases than such as are amenable to this mode of treatment."

Static Electricity.—In the treatment of exophthalmic goiter static electricity has a strong advocate in Wm. B. Snow, of New York. To use his own words, (Archives of Roentgen Ray and Allied Phenomena, September, 1908): "In the early stages of Graves' disease and of simple goiter, whether the condition is one arising from an inflammatory process or an altered metabolism, the application of the static wave current is indicated. Energetic successive contraction and relaxation, with a not too rapid discharge at the spark-gap, induces an active tissue gymnastics throughout the substance of the gland, thereby forcing out all infiltration and removing inflammatory products, and thus restoring the normal metabolism. The current is administered by placing a metal electrode over the thyroid gland, and securing it in place by bandage about the neck; or the patient may hold it in position against the thyroid with a towel. When the current is applied, the spark-gap must be just long enough to cause the tissues to vibrate energetically, but not sufficiently long to produce a tonic contraction in the sternomastoid and other muscles of the neck. This current should be administered for twenty minutes daily. By this method alone the writer has frequently seen simple goiters disappear within a few weeks. Exophthalmic cases also cease to progress or disappear, tachycardia is entirely relieved. In many cases th treated early and have since been kept under obs there has been absolutely no recurrence of the t

Leduc's Current.—Günzel describes his method o ing the intermittent electric current in the treat exophthalmic goiter, saying that the results have l cellent in nearly every case and surprisingly fine in ber. He bases the treatment on the assumption t trouble is the result of excessive irritability in the thetic system. This high frequency interrupted reduces the excitability of nerves and thus benefits ralgia, migraine, angina pectoris, lumbago, sciat rheumatoid pains even with a ten or fifteen minute tion. This current is able to induce in animals a to eral anesthesia. It also has an attenuating and influence, Günzel says, on all nervous functional ances, and this effect is particularly marked in ex mic goiter. The positive fork-shaped electrode fits goiter and sides of the neck, while the negative is ap the chest or back of the neck. He states that the excitement, the palpitation, insomnia, headaches an breathing subside in the first five to eight sitting nine or twelve the goiter and exophthalmos are m reduced, and by the end of the course of twenty o sittings, the disease, if not of too long standing, i tially improved or cured.

The *high frequency current applied with the vacu trode* has been of service in many of my cases. T electrode is applied over the thyroid gland, ten at a sitting, two or three times a week. It seems t the reduction of the size of the thyroid in each i This current weakly applied over both eyes by me binocular electrode has apparently been of marked in rapidly overcoming several cases of extreme ex mos.

D'Arsonval's Current.—Administered in the autocondensation chair, d'Arsonval's current is an efficient method of mental suggestion, but seems also to possess genuine alterative or tonic properties. In most patients the vasomotor instability is overcome, the glycosuria diminished, the nervous irritability reduced and the tachycardia relieved. Of course, the effects of this treatment are fugacious, lasting but several hours; the superimposition of effects may be accomplished by daily sittings of fifteen to twenty minutes, which method is very satisfactory, assisting toward a state of well-established improvement.

Finally, I would suggest that electricity in some form be administered to all patients if possible, and of the various forms to be employed, the two last mentioned are the most useful and the least exciting to the average patient.

VII. Psychotherapy

"The proper study of mankind is man."

An important phase of the nonsurgical management of exophthalmic goiter and one by no means to be ignored, is psychotherapy. The sensorimotor, the sympathetic, and the psychical elements of the nervous system are in a state of extremely high tension. The tremor of the outstretched fingers and the toes and also of the tongue; the markedly increased reflexes; the extreme insomnia; the high tensioned mental state of the patient as evidenced by his readiness to flare up in anger, fear, grief, and other emotions, on the slightest provocation; the ease with which lacrymation and hysteria occur; and not infrequently, the marked change in disposition, with recurrent periods of melancholia and mania;—all these present a picture of a kind of delirium, so to speak, of the various nervous centers, through the medium of the irritating thyroid substance issuing from the hyperplastic thyroid gland. We must here include a mention of the disturbed nervous control of other organs. The stomach suffers with the evidences of the nervous aberra-

tion as manifested by the typical symptoms of "
dyspepsia"; there is alteration in the tonus of tl
tines, giving rise to diarrhea, constipation, or a
alternation of the two; the excitability of the bladd
is evidenced by the frequent diurnal and nocturnal
tion; and even the sweat glands are not forgotte
most cases there is marked hyperidrosis. It may
that more than half of the symptomatology and
findings in exophthalmic goiter are traceable to t
ous system, the *central* nervous system being lar
plicated.

Psychotherapy aims primarily to influence and
the mental or inner life of the patient, and second
flexly to cause a restoration to normal of the deprav
tions of the body. That the mental and physical
interdependent, and that the neglect of the mental
is one of the important reasons for failure in the tr
of chronic affections, is strikingly emphasized in
eral survey of the results usually obtained in the tr
of exophthalmic goiter by the profession at large.

Along with the recent marked strides in medici
has been a diminished interest in the patient. The
sis of the disease, the probable pathology of the
speculations regarding prognosis, and the probab
mortem findings in the event of death, are indeed vi
portant in the interest of cold science, but the *p*
often forgotten. The mind which seeks relief of
ness and restoration to health is neglected, as a
which therapeutic efforts fall short of their aim.

The Mind in Medicine

The reasons for the study of the mind in medicin
vious when we examine the bond of relationship
between bodily and menal phenomena. Seeing s
hurt in an accident, or the sight of blood, often ca
observer to vomit or faint; the excitement of joy o
pation gives rise to loss of appetite and a state of in

in daily duties leading to indigestion and insomnia; the presence of jovial, cheerful companions at a feast will enable one to consume enormous quantities of food with impunity. Moderate sorrow increases, great sorrow checks the flow of tears; tense anxiety gives rise to cold, clammy skin; the change in quantity and quality of milk in the breast of a mother, because of emotional excitement, with consequent injury to the infant, is a common occurrence. When one has not eaten for several hours, the sight of a well-arranged display of pastries or the odor of the busy kitchen will arouse a gnawing hunger and cause a flow of saliva and gastric juice. How often have I seen the medical student, facing an examination, suddenly find himself suffering with nervous diarrhea, a splitting headache, or, as sometimes happens, mental vacuity! Who has not seen the blush of shame or modesty; and what doctor has not observed a patient's pulse rate of 70 rise to over 100 when the latter enters his office for the first time?

Conversely, the various bodily affections influence the mind in various ways. The apathy, mental dullness, hebetude, coma, or delirium caused by the various toxemias and febrile affections are matters of daily observation. The sudden loss of blood in the brain through peripheral hemorrhage results in vertigo and syncope; an increase in thyroid secretion gives rise to the alertness, the extreme cerebral hyperactivity characteristic of exophthalmic goiter; a diminution of the same secretion is conducive to the slow vocalization and tardy cerebration symptomatic of cretinism or cachexia strumiprevia, as the case may be. The drowsiness, fatigue, and somnolence following the ingestion of large quantities of food, especially meats, is the common experience of almost everyone. What "school marm" has failed to observe the close relationship existing between adenoids and mental deficiency among her pupils? And what busy doctor has not observed an occasional instance of talkative delirium following the instillation of a drop or two of atropine solution into the conjunctival sac? These and many more instances, which for lack of space we are spared the pains to enumerate, should convince one of the importance of a careful study of psychical phenomena. The physician can not be a master of the body unless he is also master of the mind, for the two are inseparable. It is not fair to compare the living human body to a boiler or locomotive, as is commonly done in our public schools, and often implied even in our colleges. The body is not merely the place where there must be maintained the proper equilibrium between construction and destruction, between repair and waste, between anabolism and catabolism. The human being has a mind which profoundly affects the entire body, and this body profoundly affects the mind in return. Man has a thinking apparatus which the machine has not; his feelings can be injured, quickened, depressed, with various bodily reflex results. Man can love and esteem, and, unfortunately, hate, and is ever desirous of being loved and esteemed by his fellows. A disturbance of the balance of man's affections, passions, or feelings is always accompanied by bodily derangements, perceptible or imperceptible, and contrariwise, bodily derangements, no matter of what nature, influence the central nervous system in varying degree.

The Ego In Health And Disease

In dealing with mind, we deal with the *ego*, or selfhood. The normal self is the great problem in the study of ethics and its offshoots—sociology, political economy and, in fact, everything involving human motive and action. No one completely reveals himself at any time. "You must eat a peck of salt with a man before you know him." The animal, the primitive man and the child are said to be more consistent in selfhood than the modern human being, as variability of mental action comes with development. How often do we hear the excuse, "I was not myself," or "I lost myself when I did that"; and when the acts calling forth such excuses pass beyond the boundary of normality (an arbitrary standard), we reach the field of mental aberration commonly expressed by suicidal and homicidal tendencies, hysteria, melancholia, and the like.

Between the dual nature of "Dr. Jekyl and Mr. Hyde" and the duality of selfhood hardly expressing itself as such in an individual of high standard of normality, there are various gradations. All human beings possess an inner and an outer self—a condition tantamount to dual personality; this is often strikingly emphasized when the inner, unpolished self is revealed in its true color, when volition is suppressed during sleep-talking or while under the influence of alcoholic or other forms of intoxication. Each self—one the nobler, the other the coarser—possesses a degree of comparative prominence and separation from the other, differing with individuals. We also find that at different times in the lives of individuals, one self, heretofore suppressed, finds ascendancy and expression over the other self, as seen when a criminal becomes a minister, an honest man a thief, a drunkard a model husband and citizen. Inspiration itself, whether religious, patriotic, or esthetic, is the expression of one at the expense of the other self.

In the consideration of the mind, we must take into account the basic temperament of the individual. Temperament is a flexible term, capable of varying definitions, but for our purpose it may be defined as that constituent of selfhood indicating by word and deed the usual type of tendency of an individual during ordinary and extraordinary circumstances. Does temperament bear a causal relationship to the production of exophthalmic goiter? We need but recall that this disease is nearly always prevalent in persons whose psychical centers are continuously on the alert, and that this state of alertness reaches its climax in the occurrence of hyperthyroidism, to respond in the affirmative. The *optimistic* temperament in which all is song and happiness,—everything in the world, from the Deity above, throughout all nature, even to the very storms and earthquakes, is good,—rarely, if ever, furnishes a case of exophthalmic goiter. The *indifferent* or "callous" temperament is also practically immune. Here, despite the absence of exuberant spirits, the individual usually lives to a ripe old age, for he is flustered by nothing; that which would worry sane persons affects this one like "water on a duck's back." Incidentally, the person with the apparently indifferent temperament is often the most useful to society, for he is capable of cool, logical judgment in the emergencies of life. The *stupid* temperament, incapable of emotionalism not because of indifference, but through deficient cerebration, is fairly immune to this disease. The stupid must not be confused with the *silly* temperament, a state of selfhood in which emotionalism—crying, giggling, depression and exhilaration—all the various moods may become prominent and alternate with little or no provocation. Among these individuals we expect and do find numerous cases of Graves' disease. But it is among those of a *hypersensitive* temperament that we find the greatest number of cases. The man or woman in this category is not necessarily of the "silly" type, as there is usually a basis for the emotional reactions. "Thin skinned" is the appellation often used as a synonym for the subject of these emotional reactions. The difficulty lies in the tendency of the individual to exaggerate the circumstances giving rise to the emotionalism. This person is suffering under a constant tension, and life to him is a perpetual succession of knocks and bumps. He is overattentive, and under the magnifying lense of his mental vision a mole hill becomes a mountain, and the circumstances giving rise to the distress is dismissed with great difficulty. The hypersensitive is related to the *pessimistic* temperament, a state of mind in which all is dark and gloomy, and the world is "going to the dogs." The pessimist and his frequent periods of exaggerated depression often tries the soul of relatives, friends and medical attendants. This class also offers many cases of exophthalmic goiter to the profession. Thus we could enumerate many other varieties of temperament and point out the degree of immunity or susceptibility to exophthalmic goiter, as the case may be. Each presents a degree of normality or abnormality when compared to the unwritten or arbitrary standard of selfhood; each involves a degree of balanced or unbalanced volition, and many, if carried to the extreme degree, lead, among other terminal states, to exophthalmic goiter or Graves' disease.

If the "normal" person's *ego* or selfhood presents no fixed character and is often a puzzle to the observer so that allowances must be made by those about him, how much more allowance must be made in the interest of the sick one who is far more prone to variations! It is for this reason that the subject of exophthalmic goiter at times deems himself a martyr to what he considers the antagonistic forces of the household,—the refusal of those about him to make the necessary allowances. Allowances within reason *should* be made, correction of his environments *must* be affected; but the patient must in course of time be made to realize that this state of antagonism is largely of his own creation,—that the world is what he makes it,—that it is indeed a good place to live in if he would but cooperate to make it so.

Sympathy and Affection

An analysis of the case of the "martyr" usually discloses a tale of lack or absence of sympathy of the world at large with his complaints. Although this mortal is surrounded by relatives and friends, he is alone—intolerably lonesome, as one on a desert isle. He is yearning for someone to whom he may impart his suffering—someone whom he may trust, to share in his misery. It is in this state of mind that the gregarious instinct,—the basis of individual and social self-preservation, asserts itself most prominently.

The common mode of treating neurasthenia, hysteria, the hysteroid and other forms of emotionalism commonly seen in exophthalmic goiter (from the ranks of which these "martyrs" arise) has been by icy sternness. "Do not sympathize with her; she must be forced into common sense. There's nothing wrong with her; she's just bluffing!" These, and similar exhortations have been the doctor's orders with respect to these unfortunate creatures. Could you quench fire with more flames, and calm an excited mob by inciting more anger? If these are impossible, so is it the height of folly, so is it cruel and inhuman further to rouse the turbulent emotions by antagonism. Efforts at logical subjugation of the patient to common sense, and at persuasion, with a view to the avoidance of further outbursts of these "fits," should be tried with intelligence, caution, and tact, and only between attacks, *i.e.*, during the intervals in which there is relatively good health, or after the patient has been sufficiently nursed back to health to be capable of calm, deliberate reflection. The nervous patients, not only women, but men also, demand not severity and frigidity of the caretakers, but the kindest charity in the method of approach; for these poor souls suffer most of all from love starvation. Such a patient's doctor, nurse, and relatives must exercise temperate judgment, patient firmness, discretion in word and deed, and an earnestness which wins the confidence of the weak one. The latter, fed on this sympathy, affection, love, soon ceases to be starved; there is a restoration of emotional stability, strength of mind and body gradually returns, and in time the patient is well and strong.

In this connection, it must be observed that the patient's habits, tendencies, petty obsessions and vices, if these exist, must be learned. Often, after confidence is secured, he or she will confide in the physician the secrets which have been torturing the mind, and which have been the cause of the difficulties. How often is it discovered that the trouble began with lack of affection on the part of one or more relatives or friends! How often, to be sure, is it the old, old story of unrequited love of the opposite sex! A confession is then a rather fortunate circumstance, for there is not only a relief of the marked mental tension, but what is most valuable, it gives the physician an opportunity immediately to endeavor to overcome the cause of the trouble by the proper psychical appeals. To quote our esteemed S. Wier Mitchell: "To confess is for some mysterious reason most profoundly human, and in weak and nervous women, this tendency is sometimes exaggerated to the actual distortion of facts. The priest hears the crime or folly of the hour, but to the physician is oftener told the long, sad tales of a whole life, its far away mistakes, its failures, and its faults. * * * The causes of breakdowns and nervous disaster, and consequent emotional disturbances and their bitter fruit are oftener to be sought in the remote past. He may dislike the quest, but he cannot avoid it. * * * The moral world of the sickbed explains in a measure some of the things that are strange in daily life, and the man who does not know sick women does not know women."

It is admitted that many of these patients are unreasonable and at times exasperating. Here again we are dealing with a sufferer requiring therapeusis of the most charitable, the most tactful, diplomatic sort. Is not this person suffering from an abnormality? If this be so, why not treat by the neutralizing, the mollifying forces of mental therapy? In fever we sponge the patient, administer cold beverages to quench thirst, overcome respiratory embarrassment by plenty of fresh air, apply an ice bag to sooth an area of congestion. Then is it not reasonable, humane, and the most natural thing to combat a mortal's mental turbulence by the calm, soothing, healing influence of sympathy and affection?

What is that which I call sympathy? It is a quality which enables one to enter dramatically into the joys and griefs and sorrows and woes of others, to comprehend what the others suffer and experience. In brief, to feel with and for the sufferer, and to be able to assist in calming the troubled waters of life by proper word and deed. Though this quality is easiest acquired by those who have themselves suffered, this is not necessarily the case. Many physicians who have not suffered greatly in body and mind, but who are endowed with a benevolent, imaginative power, feel for and with their patients, even to the extent of actual subjective suffering. Here let me sound a note of warning. As in the case of drug administration, the patient has his or her idiosyncrasies, comes from this or that social, intellectual or financial stratum, is subject to various mental peculiarities, and consequently requires careful study before actual mental therapeusis is attempted. Strict individualization is therefore the keynote in this regard. The mere poulticing of the feelings of the sufferer through a few ingratiating, stereotyped phrases, may do for the average mortal or for the weakminded creature who is so sympathy hungry as to reach for even a tiny crumb of affection; but the patient possessing average reflective powers secretly rebels against the doctor who lacks tact and diplomacy. Real sympathy can only be meted out by the student of human nature capable of individualization; each case is quite different from all the rest; the doctor's words and actions must reveal in him a keen interest, strength of purpose originating from firmness of conviction, from self-confidence which alone can gain respect.

The patient must ever be kept in courageous, hopeful, even jubilant spirits. A change of medicine, a slight change of diet, a funny story, and the never-to-be-forgotten friendly handshake on entering and leaving the sickroom, are items which often spell success and confidence.

While an *oversupply* of sympathy, affection and indulgence with the petty whims of the patient is possible and even desirable for a time, a continuance of this is not advocated when the patient is obviously improved and volition approaches the normal. When a definite state of convalescence is reached, all the suggestive powers of the medical attendant must be brought to bear in an effort to have the patient think along logical lines. Success attends these efforts in the vast majority of cases, if the physician adopts the proper mode of procedure by employing the necessary tact and diplomacy. The members of the household, especially the fond helpmeet or parent, must be instructed to cooperate in this matter. It must be firmly stated that sternness in obedience to orders shall and must characterize the treatment, and the physician must take the trouble to elucidate clearly the reasons for his stand. Regularity of sleep, rest, exercise, feeding, proper attention to bathing, the quality and quantity of foods and beverages, the kind of recreation to be indulged in, each and all must be given careful attention, lest the patient step back from a greatly improved state to his former miserable condition. To become the least bit slipshod or indifferent to the strict regimen outlined by the physician is to play with fire and invite a serious, if not fatal, relapse.

Talkative friends had better stay away in cases of hyperthyroidism. These patients are peculiarly susceptible to suggestion and suggestive influences. Such visitors are often inclined, in sympathetic attitude, to overdo matters, and in the course of conversation recall the patient's past experiences, which would manifestly be harmful. Moreover, the patient, in the presence of friends whose sincerity is limited, cannot be at ease, since he will feel that his duties as host are obligatory, and this situation, of course, is incompatible with complete physical and mental repose, and hinders convalescence.

Sexual Instinct and Balance

The term "love" may indicate an intensified degree of affection for another individual irrespective of sex, or it may imply an attraction of the opposite sex and a craving for sexual gratification. Whether we should consider the one pure and the other impure depends largely upon circumstances and the relationship of those concerned; this had better be left to the moralists for decision.

Many a nervous individual, whether hysterical, neurasthenic, or a subject of hyperthyroidism, will, when closely questioned, reveal a state of what I term "love starvation" as the starting point of the disease. Lonesome maids and bachelors living in almost total solitude are instances of this sort. The lack or deficiency of parental affection will often cause the child to become morose; an old mother will become melancholy on seeing her adult son or daughter drift away from maternal ties. Brothers, sisters, cousins, all are now and then, consciously or unconsciously, guilty of misapplication or withdrawal of the love which they are bound by blood ties to manifest, and the sufferer finds herself or himself in the doctor's office, a subject of nervousness. The sudden frigidity of friends sworn or unsworn, inconsideration of employers, an occasional slur through word or deed by an acquaintance, the boarding house mistress, or even a stranger, will in some cases be the starting point of a spell of nervousness leading to hysteria. The human being is essentially the mind; the body is quite similar to that of the lower forms of life. This mind is in its very selfishness possessed of gregarious or social cravings; in other words, the human mind yearns, lives, for affection, esteem, love of those about. There is no such thing as a real hermit. This love-craving propensity is adjusted with a fine, hairspring mechanism, so that a slight glance, a word, a gesture, results in anguish, self-torture and emotional outbursts.

But by far the most important phase of the subject is that dealing directly with the sexual life of the patient. Here the term love (as emphasized by Freud) bears directly on a consideration of sexual structure and function. If the sexual life of each nervous patient seen by the doctor on his rounds, were inquired into, what interesting information would be obtained! What a vast world of hidden disappointments, embarrassments, tortures, mortification and degradation would be revealed if strict candor were observed in these histories! And, to revert back to the subject of hyperthyroidism, how often have I seen advanced cases of this sort whose etiology may be traced back to disturbed sexual balance! Is it not obvious that if the sexual instinct can give rise to the most intense emotions, the resulting disturbance of the mental life of the individual may lead to endocrine disturbances, and since the physiology of the thyroid gland is so intimately related to that of the sexual organs, its function would be the most susceptible to derangement?

Concrete examples of this state of affairs are numerous. Take the case of a young woman with advanced exophthalmic goiter of two years' duration. She has been engaged to be married for some years prior to the onset of the disease. In the absence of other etiologic factors, what is the inference? Prolonged engagements, with their late hours and other features which we leave to the reader's imagination, are decidedly inimical to physical and mental stability. A case of this sort requires extreme tact and firmness; the lovers may be permitted to see each other once a week for an hour or two, in the presence of the household. A six months' careful treatment may result in such improvement that the couple may be permitted to marry. The young woman should be kept under observation for six months or a year longer, until the cure is affected. During this time the necessary sexual instruction should be given both husband and wife, among which must be included the use of separate sleeping chambers.

We often see an instance resulting from excessive sexual indulgence with its perpetual congestion of the pelvic organs, extreme nervous tension, and dread of the unreasonable demands of the husband. Or, the wife may be a subject of frigidity even in the presence of normal demands, and the dread of the husband's advances may have brought about her condition. Here the medical attendant should have a heart-to-heart talk with both parties and carefully but fully explain the situation without mincing words. The treatment, to be successful, must include a serious attempt at sexual equilibrium. To this end both husband and wife must be treated as the exigencies of the case demand.

Here we have an instance of vaginismus or of priapism, as the case may be; there, a case of marital maladjustment because of malformation of the sexual organs; now, a serious case of prolonged masturbation; again, a patient suffering with venereal disease or pelvic neoplasm. In each of these and in many other sexual affections which could be cited as bearing a causal relationship to thyroid hyperactivity, the attempt at restoration of normal structure and function may require the assistance of a competent gynecologist or genitourinary specialist as the case warrants.

These cases offer great difficulties, as in the usual instance the mention of sexual matters, especially if the patient be a female, renders her loath to talk freely. It must be explained to the patient that sexual organs are attributes of normality, and that it is just as proper to discuss with the doctor the organs of procreation as to discourse on the organs of digestion or respiration. It must further be explained that legitimate sexual intercourse is a *moral* act, an act sanctioned by God and Nature in the interests of race preservation. Thus the degree of false modesty is usually removed and a state of mutual confidence established. The medical attendant who knows human nature well will have little difficulty in completely revealing a sexual history which might prove of inestimable value in the interests of prompt recovery.

Psychotherapeutic Influences in the Treatment of Exophthalmic Goiter

A few influences in psychotherapy have been implied in the foregoing remarks. Although mental treatment cannot be discussed or practiced with the exactitude of mathematical precision, chiefly because of the still vague status of the science of human psychology, variations of mental activity of both physician and patient being as numerous as the grains of sand, certain deductions serving as generalizations applicable to the average case may be drawn as the basis of psychotherapy. We need not ponder long to conclude that the outstanding, the universal need is the harmonious adjustment of the patient's inner with the outer world,—the successful adaptation of internal circumstances with external environments. And the first requisite in efforts to bring this about is the necessary

Personality of the Physician

The qualifications of a physician called upon to employ psychotherapy in the management of a case of exophthalmic goiter are those capable of inspiring unconditional confidence in the patient, and a religious obedience to orders. These qualifications should serve as an entering wedge into the inner life of the patient, enabling the doctor to participate in the feelings and emotions of his charge; in short, to feel with and for the sufferer. Few physicians, and these are the eminently successful ones, are born with these qualifications. The great majority of members of the medical profession must acquire this asset sooner or later, if they are to reach a successful goal. Those doctors who fall by the wayside and blend into other pursuits of life, are those whose makeup renders it impossible to adapt itself to these vital requirements. The doctor who is an automatic prescription writer, who merely feels the pulse, observes the temperature, formulates a chemical concoction, and disappears, forgetting to devote at least as much time to the mental, the psychical construction of the patient—the doctor, in brief, who treats every patient as a "case," without an attempt to lend cheer and delight to his social atmosphere and make the sick one delight in his presence, is lacking at least 50 per cent of the qualifications of his calling. There are two phases of this matter,—first, the outward appearance of the physician, and secondly, his manner.

The necessary *outward* appearance alone may serve its purpose for a brief while; the absence of this, even though all the other qualifications exist, will fail to achieve the desired results. The outward appearance of the physician in charge of a case requiring psychotherapy must not be subject to adverse criticism. A multicolored necktie, unpolished shoes, uncreased trousers, absence of laundered cuffs, languid, unshaven features,—all or any one of these may seal a lack of confidence and respect for the doctor. I have seen a patient shrink from one who, though otherwise dressed beyond reproach, was unconscious of the fact that his collar presented a blood stain caused by a slight laceration of the skin through shaving. A medical attendant must be dressed in an up-to-date but reserved fashion. He must be neat and immaculately clean. His appearance and poise must bespeak a keen observance of physical and mental hygiene,—his features should glow with the joy of life and health,—an example to those whom he is called upon to assist.

The required *manner* of the psychotherapist is not easily acquired, but success usually attends serious efforts in this direction. He must be keenly alive with regard to the variations which present themselves in exophthalmic goiter, a disease which is rarely typical in manifestations; he must be a broadminded student of human nature and especially of the psychology of a brain continually stimulated by an excess of potent thyroid secretion surcharging the blood; he must treat his charge in much the same manner as he would a mental case, and must therefore be, in part, a sort of alienist, and as such capable, through proper suggestive influences, of bringing pressure to bear upon the necessary emotional channels with a view to inspiring complete willingness and determination to cooperate, in order to secure as prompt and complete a result as possible. The essential point, then, is implicit, unconditional confidence of the patient in the doctor, since the patient must consider his medical caretaker as his truest friend.

Not only must confidence be won, but care must be exercised to keep it alive and fresh in the patient by the happy countenance and cheerful, soothing manner of the doctor, inspiring a feeling in the patient that all is well. The physician's wits are often taxed to their utmost, because of the numerous types of temperament or personality with which he is confronted. Patients of various strata of mentality, of various degrees of culture and levels of society, presenting diverse psychical attributes, require a kind of strenuous adaptation of the medical attendant. The jolly and the indifferent, the stupid and the silly, the hypersensitive and the pessimistic, the young and the old, the capitalist and the pauper, each should find in the physician his true friend, his ideal. It is the doctor's duty to analyze each mind in order to reveal and bring to the fore the elements that best suit his purpose. As confidence and respect for the doctor increase, and the patient's volition and power of logical reasoning are improved, the favorable relation between doctor and patient must gradually become the instrument of tactful authority and discipline in the interests of permanent recovery.

In many instances the goal is difficult to attain without *extrinsic* cooperation. In other words, other factors external to the minds of doctor and patient must be taken into account, among which must be included

Correction of Social Environments

To discuss this problem of psychotherapy in detail would mean to write a handbook on social psychology. It is our purpose merely to mention a few points requiring correction, factors which serve as external circumstances maintaining the state of disharmony with internal conditions.

The patient's household is often the place of antagonism with the favorable course of events in treatment. Whether it be husband, wife, son, daughter, or relative, the close association, instead of confirming a state of contentment, of concord and happiness, often breeds a degree of contempt and chronic unconcern to feelings, most often of the ailing one,—a disgust of the strong for the complaints and foibles of the weak, and the patient becomes a helpless invalid—a "martyr" to social environments. Here also the doctor's duty is one replete with tactful authority and stern appeal to those of the houshold for hearty cooperation. He must take them into his confidence and explain that "a house divided against itself cannot stand." He must point out that though all members of a family are not of the same temperament or disposition, each possessing certain likes and dislikes regarding food, education, amusement and esthetic pleasures, causing them to seek separate places and circles during many hours of the week, engendering at times a degree of mutual indifference often leading to animosity, the properly regulated household should not only seek to avoid conflict on the issues of disagreement, but must deem it a duty to arrange for frequent moments of happy reunion. Certain hours during the week should be devoted to the purpose of mutual entertainment, of games, music, reading, and the like, so that the family as one person may enjoy itself in a harmony that spells health and life to all. It should be emphasized that each member of the family, but especially the ailing one, should have not a house, but a home to live in.

Often the *household* is just what is lacking, the subject being a maid or bachelor without friends, suffering with oppression of lonesomeness and solitude. Here the physician's task is difficult, and his mode of procedure will depend upon the nature of the individual circumstances —the patient's personality, economic resources, and the severity of the disease, with a view to advising a change of social environment. Marriage, if circumstances are favorable, or as soon as the degree of improvement renders this step safe, is the ideal change.

Occasionally a patient's difficulties are in the form of chums or friends, who, as bores or tactless diverters of mental health, consciously or unconsciously play the part of antagonistic elements to hinder recovery. It is often difficult to discover and weed out these undesirables, but sooner or later this is accomplished, again by tactful firmness so that no one need be offended. It is made known to those whose company is harmful that visitors are prohibited. At the same time a few of those whose presence is a help may be permitted about the patient, to "keep him from becoming lonesome." False and undiplomatic visitors are not only in the way, but at times bear an etiologic relationship to the incidence of the patient's affection.

Patients whose economical resources are meager and who must work for a living, seem to offer a serious problem for solution, but in reality this is not so in the usual case. Most often the wage-earner will improve more rapidly than the idler, simply because the former has very little time to become self-centered. Psychotherapy here has little to do excepting the maintenance of a state of cheerfulness and the instillation of a confidence in the future. The place of employment (assuming that the patient is strong enough to work) must be such as to offer no serious criticism in the interests of physical and mental health, and if favorable conditions do not obtain, a change must be made. Long hours, excessive physical and mental strain, poor ventilating, lighting and heating systems, dust and other impurities in the atmosphere, and last, but not least, uncongenial coworkers and exacting employers,—all these must be taken into account and avoided.

The question of long hours of work leads us to our next topic, that of

Rest and Exercise

Often the difficulty is just the reverse from the foregoing. Instead of too much work, there is nothing at all to occupy the patient's mind, excepting the doting on signs, symptoms, and the prognosis of the disease. Continuous idleness may cause more harm than a nine or ten hour day's work. In other words, complete physical rest is in most cases productive of an "overtime" state of nervous turbulence. Excepting in the event of extreme tachycardia or an organic heart lesion, complete idleness should be guarded against as inimical to the favorable course of events. The patient's mind must be occupied during several hours daily with some vocation or avocation of an interesting nature. A state of idleness in bed, for many weeks, is often enforced upon the patient by the attending physician with the view of "resting the heart." Innumerable instances of exophthalmic goiter treated in this way have led to the conclusion that a heart without organic lesions is not rested by this means. A prolonged rest in bed is not rest at all, but a means of increasing the state of physical and mental irritability. The ideal routine is the taking of a daily two hours' rest in bed after the midday meal during the period of active treatment, the remaining waking hours to be occupied in a manner indicated by the circumstances of the case.

The question of rest and exercise is further discussed in the section on hygienic treatment.

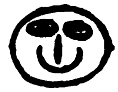
The vital need of rest for the active mental faculties brings us to the consideration of more subtle measures to be employed by the psychotherapist, the most potent of which is

Laughter

The habit of having the corners of the mouth constantly turned upward into a smile or a laugh is one of the greatest assets to the medical practitioner, as well as to the patient. A very prominent physician of Philadelphia once told me that the secret of his eminent success lay in getting all the wholesome fun he could out of practice. This disciple of Hippocrates—a picture of health—tall, robust, eyes ever gleaming with joviality, would no sooner enter the sickroom when the eyes of the patient would brighten, a smile would soon efface the lines of suffering, and within a minute or two, both doctor and patient could be heard laughing in care-free abandon over some funny story which served the purpose of the time. This clever M. D. was up to the minute on the literature of the day, could discourse with rare intelligence on the merits of contemporary authors, and above all, possessed an enviable stock of funny stories and jokes which, though not included in the materia medica, often far surpassed it in therapeutic efficacy. While an excellent physician, this man, in "getting fun out of practice," had secured more friends than any two ultra scientific doctors I have ever known.

Laughter is more contagious than measles, and in possessing no rash, is infinitely more useful. Laughter loves company and is therefore a powerful cementer of social ties. "Laugh and the world laughs with you" is a truism worthy of deeper contemplation. The world not only laughs with you, but the world wants to know you, to love you, if you but laugh. The world laughs with you not because your laugh is the result of something extremely witty, humorous, or ludicrous, but because the world loves to laugh for the sake of laughing, because laughing is a pleasurable act giving rise to a state of agreeableness of body and mind. Need we insist that laughter dispels gloom, inspires optimism, imbues the spirits with the joy of life? Need we recall that laughter increases appetite, improves digestion and assimilation, favors healthful, refreshing sleep, and improves physical and mental usefulness? And wholesome laughter, being an expression of love of fellow-creatures,—does it not radiate fraternity—a fellowship tending to diminish worldly discord and enhance the unification of the human family?

The subject of exophthalmic goiter is the picture of perpetual gloom, fright, introspection, melancholy and other mental states far removed from the glow of gladness. The substitution of a mouth whose corners are turned up for that of constant bleakness with corners depressed, is a process which should begin at once in the treatment of Graves' disease. Since laughter is gladness and gladness is conducive to well-being, laughter is a great tissue builder, so that "laugh and grow fat" is not a mere aphorism. In exophthalmic goiter, the sooner the fattening begins, the more prompt the cure.

The medical attendant must himself be the picture of joviality and optimism in the presence of a case of exophthalmic goiter, if he is to impart gladness and smiles to his charge. The serenity of the doctor's countenance must not amount to or be capable of being interpreted into terms of cold, scientific curiosity and indifference to subjective history and complaints. He should appear serene, but it should be a smiling serenity, a face of hope "writ large." The patient has gone the rounds and seen many doctors before; operations have been suggested—perhaps she has already submitted to one, perchance to two surgical procedures, and she is not only in a state of exaggerated physical and mental depression, but has lost confidence in medical men as a whole. Some one has sent her to you as a last resort. At first she refuses to bother, preferring to live it out to the end. But she is finally prevailed upon to see you, and here she is, a frail, helpless, hopeless, trembling, throbbing creature, her bulging eyes bespeaking almost a defiance against your potentiality to assist. She happens to be a girl of eighteen, accompanied by her father. You discuss the weather for a moment and smiling sympathetically, you ask her to tell you slowly her complaints. As you patiently listen, you jot down the salient features of her narration and turn to her parent for further history. Then, with smiling countenance, and soft, modulated voice, you question patient and father until the history is complete, always guarding against overburdening the sufferer with too rapid questioning. Then, as a parent tenderly undertaking the care of a child, the necessary physical examination is made. By this time, the patient begins to feel at home in your presence,—nay, more than at home. There is something about your every word and move that inspires that of which she has great need—confidence. She feels that she has reached a medical man who wants to help her, and when you smilingly ask her if she will cooperate in the measures you outline, assuring her of the great prospects of recovery, she promises, almost with enthusiasm. After you have given them the necessary instructions, you cheerfully bid patient and parent a warm *au revoir*, and with fatherly handshake inform them when to call again. One week, two, three weeks pass by, and your patient begins to improve in every respect. At the termination of a month, although she has gained 8 pounds in weight, appears and feels better, she is still morose and melancholy, and you feel that a cheerful attitude would mean more rapid progress. This time, when she appears with her father in your office, you are determined that smiles *must* predominate. "My child," you say, "you are getting better, aren't you?" "Yes, but I am not quite well yet. I still have some diarrhea, and I don't weigh quite enough, and I get weak when I begin to do anything • • •" "Hold on a minute," you interpose. "You have been an invalid for nearly two years—do you expect to get well in a month?" "No, I suppose not," she answers moodily, "but I can't get along with my sisters at home,—they annoy me; and I get crying spells and can't eat." "Now look here," you say kindly but firmly, looking straight into her eyes, "if you do not turn the corners of your mouth upward into a smile, I shall refuse to treat you any longer." "Oh, doctor, don't say that," she exclaims, somewhat startled. "I mean what I say," you insist. "If I cannot get your help to cure you, I shall give you up. I want to convert you from a very sick girl to a well little friend, and all that is now lacking is smiles and laughter." Your face broadens out into a laugh as you say: "Now come close to my desk, both of you,—father and daughter, and see what I mean." On a prescription blank you draw this diagram: "This is what you look like, Helen," you say; "now, when you leave this office and forevermore, you must look like this!" You draw this diagram alongside the other: Helen begins to giggle, then laugh,—the first real change of countenance in two years. "Now, Helen, take these along, and spend an hour a day drawing these lines, to show me what a wonderful artist you can be!" Father and daughter depart in jovial mood. The patient thrives rapidly, and within eight months you discharge her strong, well, happy, better in every way than she had ever been before, and your life long friend. On the day when you discharge your Helen, her father takes you aside and whispers into your ear: "Do you know, doctor, she is the most amiable child in the family, —and you should see her eat! Also it may interest you to know that she is still drawing those faces and teaching every one else the art. She is especially fond of this one." He takes a piece of paper out of his pocket to illustrate his remark, and it discloses the diagram expressing Helen's present mood: 

Among other means of dispersing introspection and encouraging the development of a normal mental view of the world and its contents, is the subtle harmonizing influence of

Music

The influence of music on the nervous system is undoubtedly due to the frequency, altitude, and especially the rhythm of the sound waves. All nature is motion, and all motion is rhythmical in character. Rhythm is a fundamental law of progression and metamorphosis. Music is salutary because its sound waves consist of regular, even, rhythmical vibration, which favorably influences the higher nervous centers, and reflexly, the various organs through the sympathetic nervous system, thus improving appetite, digestion, assimilation, and nutrition. Properly selected music then, may be advantageously employed as a supplement to other therapeutic measures in all conditions in which the nervous system is largely implicated. As disease is really a departure from the proper rhythm of molecular changes of cellular structure, music, insinuating its order and rhythm upon arrhythmic biologic processes, is a potent accessory factor in the armamentarium of the psychotherapist. This has been recognized of late years in clinics throughout the world, as evidenced by the institution of music clinics for nervous affections in sanatoriums in France, Germany, and elsewhere.

Music can sway all living things endowed with a central nervous system. The more highly organized the nervous system, the more profound this influence, until in man, music becomes the physic for the soul, raising it above the gross reality of tangible trials and tribulations, leading the subject on to ideational vistas of superstructural formation, not unlike a pleasant dream state. Music under such conditions fills the niche to complete the regimen of treatment outlined by the medical attendant, and is often the means of entering most deeply into the mental life of the patient when other measures fall short of their purpose.

Music seems to have a special predilection for the will of the listener, overcoming stubbornness and substituting an ability to reason logically to an extent equalled only by the effects of a powerful sermon. As the will of the subject of exophthalmic goiter is profoundly depressed and often capricious beyond reason, music, although the most severely abstract of arts, is often capable, through its very subtlety of speech, of giving support to the weakness, rationality to the stream of consciousness, and serves to improve the moral backbone of the case in question.

It is to be remembered that here also individualization is essential. Music must be prescribed with reference to its quality, quantity, duration, idiosyncrasies of the patient, and the prevailing environments. Some kinds of music exert a universal influence over the audience which, as one man, is carried away in an ecstatic dream to Utopian lands and the realization of cherished hopes: the grossness of earth's reality, its knocks and pains are effaced; the listener loves the present, looks forward with extreme joy to future possibilities and glorious accomplishments. Such is possibly the effect of Beethoven's "Fifth Symphony" and some parts of his "Moonlight Sonata." Other compositions differ in physiologic effect. Schubert's "Unfinished Symphony" exerts the pleasurable effect of a somnolent state, not unlike the influence of a moderate dose of morphine. The same may be said of Schubert's famous "Serenade," although this leaves in addition, a tinge of sadness. Wagner's music, especially the "Pilgrim's Chorus" from "Tannhäuser" is most often a potent stimulant raising the spirits from their haven of helplessness to fill the patient with firm determination to do and win. But some compositions, on the other hand, may do a little harm. Drigo's "Harlequin's Serenade," though an infinitely beautiful selection, will cause weakminded individuals a degree of sadness which may lead to lacrymation. The same, to a lesser degree, may be said of Massenet's "Elégie." While occasionally a "good cry" results in a beneficial reaction, we must, in general, seek to produce not tears, but smiles of contentment in our musical program. Moreover, not all our patients are capable of appreciating the classics. Some grow impatient with the slow, steady progress of a theme, such as occurs in Beethoven's works; others are totally devoid of this form of esthetic appreciation; still others have decisive inclinations for such conglomerations of notes found under the heading of "Jazz"—the prototype in sound of "cubism" in art. Shall we deprive these mortals of the pleasure of the popular ballad, dance music, and even "Jazz?" Decidedly not, if this is seen to assist recovery. The patient who is inappreciative of the classics has just as much right to his standard as the cultured individual has to his, and we must admit that it is really difficult to prove which standard has the greater right to exist.

Music has a place in the nonsurgical management of exophthalmic goiter. Although most patients, perhaps we should say all patients, can get along without music, we must not omit this form of mental treatment when it is available. The tachycardia, the emotional excitation, the general nervousness, and the various functions of the body which are in a state of overactivity through the stimulus of the thyroid toxemia are held in abeyance, and the greater the susceptibility of the patient to music, the more grateful the effects. Though the effects, to be sure, are evanescent in character, the frequent administration of the necessary dosage and quality of this remedial agent will, as in the case of most drugs, create an overlapping and accumulation of results so that sooner or later, concomitantly with the influences exerted by other nonsurgical procedures employed, permanence of improvement is attained.

However, music is not alone in its ability to engage the mind in passive meditation. There are other, even more accessible methods to be employed, among which is a prescribed plan of

Reading, Lectures and Conversation

Here also, we must insist on individualization, as we must take into account not only the type of patient, but the proper selection of material to be employed in our treatment. The patient may be permitted to do the reading, or, he may listen to someone else whose voice and interpretation may furnish pleasure and mental repose. Because of the condition of the eyes and nervous system, the patient should never be permitted to read small print, or in an improper light or position, or for too long a time.

Representation in reading is capable of calling forth nearly every emotion—stimulation, depression, smiles, sympathy, scorn, and the like, as well as a feeling of the esthetic delight experienced from music and art. It is for this reason that a careful selection should be made by the medical attendant of the reading matter to be permitted the patient. Newspapers should be prohibited, as their contents are often too markedly depressing for one whose emotions are overalert. Mystery stories, tragedies, tales involving extreme suspense, and the like, should also be forbidden. Reading matter should be of light, wholesome, cheerful character,—clean and refreshing throughout. We cannot recommend too highly certain delightfully humorous selections as repre-

sented by "Tartarin of Tarascon" by Daudet; nearl
the works of Mark Twain and of Jerome K. Jerom
cially "Three Men in a Boat" by the latter; "Kipps,'
G. Wells; "The Laughing Muse," by Guiterman;
those who are fond of Shakespeare, such plays a
Comedy of Errors," "Twelfth Night," and "The Ta
the Shrew." Some subjects, however, find themselve
best mood when reading the modern short story of r
or witty trend, as found in the short story magazin
allowances must here be made, as is done in the case
who can not adapt themselves to an appreciation of
music.

Attendance at lectures and sermons with or
screen illustrations may be permitted at the discr
the medical attendant, and they are subject to the s
marks as those which cover the question of readin
topic must be of a cheerful, inspiring, elevating t
must not be capable of fatiguing the listener.

Conversation, especially table talk, is a consider
importance. Those participating in it should be in
to speak in a soft tone of voice, never to jar the
nerves by violent gestures and phrases, and abov
discuss only those topics which would not arouse an
the emotions. The narration of a funny incident
recitation of a humorous selection are always in pl
these patients are usually of hypersensitive natu
should be permitted to participate not only as goo
ers, but should be encouraged actively to take part i
able conversation, in order to forget themselves. T
tion of the conversation should always be taken
count.

Attendance at the theater may be permitted with
gard to conditions and circumstances herein implie

In concluding the discussion of the measures wh
be employed by the psychotherapist for the purpose
inating the emotionalism of the subject of exophtha
ter, mention may be made of certain forms of

Miscellaneous Esthetic Recreation

Among other esthetic pleasures which appeal to the emotions and favorably influence their balance, are an occasional visit to an art gallery, a trip to some lovely country spot for the contemplation of nature's beauties, or even an occasional leisurely trip through the large city stores, that the eye may note and admire the modern wonders of man's handicraft in clothes, ornamentation, and the like. Here we obtain via the visual apparatus what music offers through the sense of hearing,—a primary central thrill of pleasure with a secondary reflex reverberation in the various organs of the body. These trips should be taken only after a sufficient degree of recovery is attained. William James thus sums up this question: "Esthetic emotion, *pure* and *simple,* the pleasure given us by certain lines and masses, and combinations of colors and sounds, is an absolutely sensational experience, and optical or auricular feeling that is primary. * * * To this simple primary and immediate pleasure in certain pure sensations and harmonious combinations of them, there may, it is true, be *added* secondary pleasures; and in the practical enjoyment of works of art by the masses of mankind, these secondary pleasures play a great part. The more *classic* one's taste is, however, the less relatively important are the secondary pleasures felt to be in comparison with those of the primary sensation as it comes in."

It can be seen that the foregoing topics as phases of psychotherapy were discussed with a view to pointing out some of the available means at hand in the interests of the

Maintenance of the Patient's Mental Equanimity

There is not only a state of discord between the patient's mind and his body, but this discord also extends outwardly and includes the world at large. The subject of exophthalmic goiter is at odds, so to speak, not only with himself, but frequently with the whole universe as well. For this reason, the physician often finds it difficult to hold his case for a time sufficiently long to enable him to bring about a satisfactory state of rationality. Not a small percentage of cases present this problem during the transitional period, *i. e.,* between the first consultation with the subject and the occurrence of results evident in and to the patient. Even in the presence of the remarkably adequate personality of the physician, and indeed, even after the beginning of apparent improvement, a slight relapse in the patient's mental status may lose him to the medical attendant. It can readily be seen then, that psychotherapeutic measures must at first include an effort to obtain as near as possible a state of equilibrium or harmony between patient and doctor, in order that this dangerous transition period be overcome. This point can not be too strongly emphasized. The question becomes one of mental reconstruction or change of mental vision in the patient.

The principle underlying or governing the art of psychotherapy is suggestion. A suggestion is an idea capable of suppressing or engendering another idea. All human life is permeated with suggestion: social existence, politics, business, the arts and sciences, and religion. The greater the amount of education of the individual or the greater the amount of native mental stability in a patient, the less susceptible he is to suggestion. On the contrary, the lesser the degree of worldly knowledge and inherent common sense, the more likely the subject is to respond promptly to suggestive influences. Patients also differ in accordance with the kind of temperament characterizing their makeup, the presence or absence of morbid obsessions, and the mood at the time suggestive influences are attempted. Also, fatigue, the possible influence of stimulating or depressing drugs at the time of the séance, and even the prevailing weather must be taken into account.

Suggestion is really a process of filling the subject's mind with strong motives to impel action favorable to the attainment of the desired goal. Speaking strictly in terms of human psychology without going into detail, it may be said that the motives most frequently obtainable to impel action are seven in number: self-preservation, which is recognized as the first law of nature; property, which is akin to the instinct of acquisitiveness; power, or the keen desire to sway others; reputation, where the patient acts in accordance with suggestion because it will maintain his good name; sentiment, affection, and taste. The patient's dearest desires and cherished hopes must be discovered, and there must also be a revelation of other weak and strong points of the mental construction. Not only must conviction be employed in the process of suggestion, but what is eminently more powerful, persuasion. The patient must be put in a state of mind in which he is convinced that there is something good to live for, and must be persuaded to begin *now* to so think and act that this awaiting good shall be forthcoming as quickly as possible.

In conclusion, we may state that in cases of Graves' disease requiring energetic psychotherapeutic measures, the doctor's task is not an enviable one, but is frought with stubborn obstacles, tedious trials and a continuous vigilance. The results obtained, however, more than compensate for the pains expended. We medical men, ordained to minister to our fellows from the first cry of life, through infancy, childhood, puberty, adolescence, manhood and womanhood, even to the sigh of the parting breath, must ever bear in mind the psychic factor—the mind, as deserving of quite as much consideration in the alleviation of suffering, as the body. The restriction of the use of drugs to cases primarily organic in nature, the administration of proper doses of sympathy, smiles, encouraging demeanor, and an attempt to reconcile cause and effect by sane efforts, although this entails a psychologic appeal to husband, wife, parent, or friend, as the case may be,—this is truly the field of the physician who aims to make his life's work replete with happiness to self and those whom he is called to assist.

Such a man, a past master in the understanding o ished human character and temperament, of the its extreme trials, feelings, and passions, suppres expressed, stands out from human society as a dist tity, and is esteemed and respected by his fellows a perman.

CHAPTER XI

A FEW CASE HISTORIES

The profession at large is now, more than ever before, prone to consider seriously nonsurgical procedures in the treatment of hyperthyroidism. The reasons for this attitude are legion. The high mortality rate in advanced cases, the uncertainty of surgeons regarding what mode of procedure to adopt, selecting now total thyroidectomy, now sympathectomy, again ligation of one or more vessels, here thymectomy, there subtotal resection, and again, a combination of these operations,—all these, with the marked lack of conclusive proof of complete surgical cure of the disease, have resulted in considerable diminution of confidence in surgical intervention in this disease. Moreover, the numerous mishaps incident to or resulting from surgery, *e. g.*, the accidental removal of the parathyroids followed by tetany,—the removal of too much thyroid tissue with subsequent myxedema, the wounding of the recurrent laryngeal nerve with paralysis of the vocal cords, and such occurrences as status lymphaticus, postoperative acute exacerbation of hyperthyroidism, and the fact that surgeons guard themselves in word and deed by a more conservative attitude than formerly,—all these seem to indicate that before long the surgeon will yield this field to the internist. Not only does the patient fail to secure relief as a reward for the danger she has reconciled herself to undergo and the scar she has consented to bear during the remainder of her existence, but the frequent regeneration of the goiter itself leads to a multiplicity of operations with a renewal of all the dangers incident to the primary operation.

How often are the surgeons disappointed when confronted with a patient suffering with all the symptoms of exophthalmic goiter but three or four months after they had operated upon the case which they had discharged cured! How often is the surgeon obliged to operate the second time, yes, and even the third time, with similar results! And in consequence of these unsuccessful surgical procedures, how often is the unfortunate patient so completely devitalized that resistance is reduced to almost *nil.* Consideration of these facts gleaned from the practical experiences of all busy practitioners and especially the observations of men who are interested in thyroid therapy, lead to the conclusion that whatever the treatment, surgery is not the cure of exophthalmic goiter.

The following cases, selected at random from the author's records, are illustrative of the potentiality for cure of exophthalmic goiter by nonsurgical measures.

CASE I*—S. B., aged thirty-four, salesman. Appeared in my office on January 10, 1913, complaining of gradually increasing "fullness in the neck," which he had first noticed a month before, when his collars became too tight. He also complained of recurrent irritation of the larynx with nonproductive cough, excitability, nervousness, insomnia, hyperidosis, anorexia, feeling of weakness in the lower limbs, progressive loss of weight and strength.

Family History.—Negative.

Social History.—Nothing of importance.

Past Medical History.—Important features were typhoid at eighteen, from which an uneventful recovery was made within nine weeks. He suffered with attacks of acute follicular tonsillitis, once or twice annually. He had at this time, an occasional period of gastrointestinal sluggishness characterized by impaired appetite, sense of gastric distension, and constipation of moderate degree. During the past four years, he had been suffering with a slight rectal discomfort because of internal hemorrhoids.

Present Illness.—About two months previous to this time, patient received word that his mother over in Germany died suddenly. He worried over this so intensely that he was unable to concentrate his mind on his daily duties. His grief occasioned insomnia, failing appetite, and mental depression. A week or ten days later his nervousness was so extreme that his wife remarked that he acted strangely and urged him to consult a doctor. His neck became thickened in front so that he was obliged to buy collars a size larger in order to feel comfortable. At this time, a slight stare in his eyes was noticed. He began to experience occasional moments of dyspnea on the slightest exertion, and found it rather difficult to continue his daily duties where he was employed. Sleep became not only restless, but some nights rather fatiguing, as he was obliged to rise three or four times because of bladder irritation and inability to retain urine. At times he felt as though his "mind were running off with him," and at other times he felt like crying. His tongue had been slightly coated, and since the inception of this illness, he had rarely experienced real hunger. Food was distasteful to him, not only because of anorexia, but because he feared to eat by reason of the gastric discomfort shortly afterwards. The bowels were irregular in function, moderate constipation alternating with diarrhea. During the past few days he had been troubled with palpitation, especially on retiring and lying on the left side. He experienced the same sensation when slightly excited and on slight physical exertion. For the past week his skin presented irregular blotches of erythema almost daily, which disappeared within an hour or two. Every afternoon and evening there had been drenching sweats to the extent that, when at home, he was obliged to change his underclothes frequently. He claimed that three weeks previous to this time his weight was 152 pounds.

---

*Cases I, II, and III appeared in an article entitled, "Successful Therapy of Exophthalmic Goiter" (New York Medical Journal, February 22, 1919).

Physical Examination.—Patient was a fairly well-nourished man, slightly plethoric, about 5 feet 6 inches in height, weighing 134 pounds. He appeared slightly anxious and rather nervous, with an occasional twitch of one or the other limb indicating peripheral motor hyperactivity. *Skin*: somewhat blotchy in appearance, veins unduly prominent, especially those of the neck and chest, texture of the skin unduly soft and moist, dermographia easily obtained. No scars or edema. *Glands*: lymphatic glands normal. *Head and Scalp*: practically normal. *Eyes*: slight exophthalmos distinctly observable; Stellwag's sign inconstant; Dalrymple's sign slightly present over left eye; Von Graefe's sign present in both eyes; pupils reacted well to light; accommodation reaction slightly lagging; the Moe-

[illegible] [illegible] diminution of convergence present; extraocular movements normal. Conjunctiva presented slightly dusky congestion. [illegible] [illegible]: slight congestion of mucous membrane. [illegible] increased and congested, moderate [illegible] of [illegible] in [illegible]. *Lips*: slightly cyanotic. *Gums*: slightly paler than normal. *Teeth*: several missing, and in general required considerable repairing. *Tongue*: a coarse tremor on protrusion; was moist and presented slightly whitish coat. *Throat*: chronically congested; tonsils larger than normal, appeared diseased and [illegible] with numerous follicles; pharynx presented a typical smoker's sore throat. *Neck*: Thicker and shorter than normal, presenting well-marked carotid and jugular pulsations. Greatest circumference of neck 14¾ inches. Thyroid gland prominent, especially at isthmus. While no distinct evidences of goiter were observable at a distance, on close view the outline of the thyroid was seen. On palpation the isthmus and to a lesser extent both horns of the thyroid gland were denser and fuller than normal, deep palpation eliciting tenderness. Auscultation over thyroid area, especially over horns, revealed a soft, slight, systolic bruit. *Chest*: inspection, shape normal; respiratory expansion 2½ inches; apical impulse seen in sixth left interspace in midclavicular line. There was slight prominence of the larger veins. Palpation confirmed inspection regarding the location of the cardiac apex. The heart beats appeared more frequent and energetic than normal. Percussion revealed moderate cardiac hypertrophy, the left border extending to within an inch of the left anterior axillary line. Tactile fremitus normal, excepting over both supra- and infraclavicular regions, where there was slight increase. *Pulse*: frequency 86 per minute; slightly dicrotic; fair volume; moderate tension; regular and rhythmical. Percussion revealed slight impairment of resonance over apices, anterior and posterior. On auscultation first apical sound was dull and booming, presenting slight systolic prolongation which, however, did not amount to a murmur. Second apical sound apparently weaker than normal. The second aortic sound sharp and clicking. Second pulmonic sound practically normal. With the exception of slight harshness of breath sounds over both apices, respiratory sounds were normal. Vocal fremitus slightly increased over apices. *Abdomen*: somewhat more prominent than normal; slight distention of superficial veins; no tenderness; moderate tympanitis over gastric area. *Limbs*: somewhat emaciated; lower limbs presented enlarged veins. There was a fine tremor of the outstretched fingers, least marked in thumbs, most marked in middle and ring fingers. The outstretched toes did not present this tremor. *Nervous System*: patient appeared rather anxious and fidgety. An occasional shrug of the shoulder was noticed during conversation. He responded promptly to questions and was in every way rational. Tendon reflexes hyperacute.

Treatment

Hygienic.—Patient was not ordered to discontinue his vocation. He was instructed to avail himself of a maximum of fresh air and rest while at home, and to take a lukewarm bath every night just before bedtime. He was warned against any undue physical or mental excitation. This was also mentioned to his wife, who was urged fully to cooperate in the treatment and so to govern the household as to render the home environments as tranquil as possible. Reading the daily newspaper was forbidden on account of its exciting contents. He was instructed to obtain a maximum of eight hours' sleep, to keep away from moving picture shows, and to discourage the visits of sympathetic friends. He was ordered to have the dentist attend to his teeth at once.

Dietetic.—Animal foods were reduced to a minimum; he was permitted a small portion of white meat of chicken once or twice a week, if desired. The main dietary consisted of milk, butter milk, sweet cream, sour cream, cottage cheese and cream cheese, eggs, plenty of bread and butter, cereals, potatoes, soups (rice, barley, vegetable, noodle, potato,—without meat extractives), vegetables and fruit in season. The following substances were interdicted: Tea, coffee, cocoa, ice water, carbonated waters, alcoholic beverages, tobacco in any form, the various spices and condiments of the table, lard and the various greasy substances, pastries and sweetmeats, strawberries, raspberries, huckleberries, watermelon, cantaloupe, bananas, and the various canned goods. He was ordered to masticate his food thoroughly, never to overload his stomach, and if possible, to eat five or six partial meals rather than three full meals a day.

Medicinal.—Patient was ordered to take a teaspoonful of sodium phosphate in a glass of water an hour before breakfast daily. Locally he was given the following:

℞ Camphor-Menthol ʒ ss
Tr. Belladonnæ ʒ iii
Tr. Iodi q. s. ad. ℥ iss
This was to be painted on lightly every night over the thyroid area.

He was given the following capsule:

℞ Quinina hydrobrom. gr. v
Ext. glandulæ suprarenalis gr. ii
Ferri arsenias gr. 1/12
S.—In capsule, t. i. d. p. c.

Within four weeks this patient felt very much better, and all that remained of the goiter was a slight prominence of the left lobe. The pulse was 80, weight increased 5 pounds; he said he was less nervous and slept better. Exophthalmos and tremor, however, were unimproved. Instead of the previous capsule, he was now given the following prescription:

℞ Quinina hydrobrom. gr. v
Ferri arsenias gr. 1/12
S.—In capsule t. i. d. p. c.

This was continued for one month or until March 10, 1913, at which time he weighed 145 pounds, a gain of 9 pounds, and said he felt entirely well. Pulse 70; exophthalmos hardly perceptible, tremor almost gone; neck practically normal; excepting a slight fullness of left lobe. Patient looked cheerful and healthy. All previous local and internal medication was stopped, and he was now placed on a capsule of quinine hydrobromate gr. v, to be taken four times daily, and instructed to return in a month. He returned in April, 1913, a normal man, with no further evidences of hyperthyroidism. To secure him against relapse, I ordered him to report to me every month until he had been under my care for a year, during which time he continued to take the quinine hydrobromate. In January, 1914, I discharged him, weighing 150 pounds. All treatment was discontinued. At this writing there has been no return of any evidences of hyperthyroidism.

Remarks.—This was an early case, and as such responded very promptly to therapeusis.

CASE II.—Mrs. M. H., aged thirty-seven, 5 feet 3 inches in height, weight 97 pounds, was sent to me on July 21, 1914. She had been given the rest cure and milk diet for three months, and in her own words, "had spent about $2,000 trying to get well, but got worse." Operation was suggested by several men, but she declared that she would rather die than be operated on. She appeared pale, thin, nervous, scared-looking, and did not seem to care whether life would hold out for her or not.

Chief Complaints.—Extreme bulging of the eyes with inability to close them, precordial distress and palpitation, incapacity for domestic duties, extreme weakness, very distressing indigestion, loss in weight, insomnia.

Family History.—Did not present hereditary tendency to thyroid abnormalities. No history of tuberculosis, carcinoma, epilepsy, insanity and cardiorenal disturbances.

Social History.—Married at twenty-one; six children; no miscarriages. There was no discernible enlargement of thyroid during pregnancy. Took five or six cups of coffee daily, also plenty of seltzer water. Was very fond of meats, eating animal foods two or three times daily. Was in the habit of using the spices and condiments, *i.e.,* pepper, mustard, vinegar, etc. During the past several years, had been working very hard to assist her husband in building up a general clothing business while at the same time performing her household duties. She therefore did not find it possible to avail herself of the proper systematic rest and regularity of meals, always eating rapidly and hurrying away to the store. Menstruation began at thirteen and was always normal in occurrence, quantity, and duration. Moderate discomfort of short duration before and during menstruation.

Past Medical History.—Had most of the diseases of childhood, although she did not know exactly the nature of those diseases. Did not recall having had scarlet fever or diphtheria. Several years previous to this time, she suffered with an attack of acute articular rheumatism, which kept her in bed for two weeks. She had, from that time on, frequent attacks of subacute rheumatic pains in the joints, especially before and during change of temperature and humidity. She had never felt well since her rheumatic attack; always complained of shortness of breath and occasional precordial discomfort. During the past two or three years she had been suffering with almost constant digestive disturbances, which condition was diagnosed by her family physician as nervous dyspepsia. Attacks were characterized by pain shortly after eating, marked sense of distention of the stomach, sour eructations an hour or two after meals, occasional vomiting. In brief, her gastric discomfort was so great during an attack that she feared to eat.

Present Illness.—Eighteen months before this time, patient was taken with what was termed a "nervous breakdown." There was palpitation, marked exacerbation of her gastric disturbance, distressing insomnia, fullness of the neck over the thyroid gland, gradually increasing bulging of the eyes, profuse perspiration, hysterical outbreaks, very rapid loss in weight, and total loss of appetite. She remarked that every once in a while she felt as though her mind were giving way and dreaded the moment when she would be sent to a lunatic asylum. This, she stated, was more troublesome to her than any of her symptoms, and she begged to be informed whether she would become insane. Her family physician prescribed tonics, a rest, and other measures calculated to overcome her nervous breakdown, despite all of which she became progressively worse. Finding that her loss in weight was becoming alarming and her strength was fast leaving her, she consulted a Philadelphia physician who placed her in the hospital for several weeks' complete rest cure. There, although at first apparently improved, her condition soon became still further aggravated, and she consulted an eminent surgeon. Immediate operation was advised, but the patient refused to consider this. She then consulted an eminent nerve specialist who, after unsuccessful treatment for a brief while, advised operation. She left him and consulted several more doctors with the same results. Finally, a physician on whom she called suggested that she see me for an opinion.

She told me that for over six months she had been obliged to cover her eyes with small pieces of flannel when retiring for the night, because the eyelids did not close over the eyeballs and, thus exposed, the ocular conjunctiva became irritated. She had not had a good night's sleep for more than a year because of the palpitation, the drenching night sweats, bladder irritation, and the extreme restlessness. She had lost 20 pounds in weight during this illness. In addition to all these complaints, her rheumatic pains had recently been becoming more severe, and at times she was unable to move about.

Physical Examination.—Patient was a small-statured, thin, nervous-looking white woman, who, though rational and fairly intelligent, seemed to lack continuity of thought in her remarks, rambling along in the description of her condition until fatigued, when she rested a while and continued on. Finally, after having given in great detail all her data, she stopped, and I was enabled to obtain her history systematically. Her eyes were almost popping out of her head and her neck was rather full, standing out in sharp contrast to the rest of her emaciated body. Her cheeks were hollow, her expression anxious and somewhat frightened, and as she sat in my office, there was a perceptible, rhythmical nodding of the head and even of the shoulders, corresponding to the cardiac cycles. *Skin*: somewhat oily and dusky in appearance; soft, thin, moist to the touch; dermographia easily obtainable. Aside from an occasional small papule, there were no eruptions nor scars. Moderate edema of ankles, extending upward to as far as the knee-joint, was present. *Glands*: lymphatic glands practically normal. *Head and Scalp*: negative, excepting for a tendency toward baldness. Patient informed me that since she had been ill, her hair had been falling out very rapidly. *Eyes*: exophthalmos very marked, greater on the right side. Stellwag's, Dalrymple's, Moebius' and Von Graefe's signs very distinct. Pupils reacted normally to light. Reaction to accommodation was lagging; extraocular movements fair. Eyes were tender and when walking in sunlight somewhat painful: Eyelids, especially the right, closed to within ⅜ of an inch of coaptation, so that the patient obliged to protect her eyes during sleep by means of a p of cloth which was laid over them at bedtime. Conj tivæ moderately congested. This applied also to the oc conjunctiva which presented numerous dilated blood ves coursing through the sclera. *Nose*: slightly conges *Lips*: dry and cyanotic. *Gums*: slightly cyanotic. *Te* well taken care of, presenting evidences of excellent de attention. *Tongue*: moist and slightly coated with a w ish layer; was protruded with a tremor. *Throat*: slight gestion present. Tonsils moderately enlarged and appea chronically diseased. Pharynx practically normal. *N* emaciated and apparently elongated, excepting over roid gland, where there was considerable fullness. Car and jugular pulsations were evident. Superficial veins (thyroid were seen and were rather dilated. Greatest cumference of neck 14 inches. Thyroid gland unifor enlarged and almost boggy, appearing as a diffused ante swelling. There seemed to be no lines of demarkation tween isthmus and horns of the thyroid. Deep palpa elicited tenderness. Auscultation revealed a harsh syst and softer diastolic bruit. *Chest*: inspection: marked e ciation, diminished anteroposterior diameter, respirat expansion 1½ inches. Apical impulse sixth left intersp near anterior axillary line; it was diffuse, extending ov radius of 2 to 3 inches. Palpation confirmed locatio cardiac apex. There was a slight systolic thrill discern over precordial area. Pulse 120 per minute, irregular, rhythmical, low tension, poor volume. Tactile frem practically normal over entire pulmonary area. Percuss showed heart was uniformly enlarged, the left border rea ing the anterior axillary line. There was slight imp ment of pulmonary resonance over the apices. Auscultat revealed first apical sound replaced by a soft, blowing m mur which was transmitted into the left axillary space around to the scapula. Second apical sound was sh and weaker than normal. Both sounds over the base the heart were weak and at times indistinct. The tric pid sound was also indistinct, apparently replaced b soft murmur. Respiratory sounds were practically nor everywhere excepting over both apices where the bre sounds were somewhat exaggerated. Here also vocal mitus was increased. *Abdomen*: There was slight enter tosis evident; also the usual evidences of frequent pregnancies. Tenderness over gastric area; slight prominence of superficial veins. *Limbs*: lower limbs edematous from ankles to knee-joints. Superficial veins moderately prominent. Upper limbs presented nothing abnormal. Typical tremor of the outstretched fingers, less marked of the toes. *Nervous System*: patient had the physiognomy of perpetual fright characteristic of exophthalmic goiter. The history of occasional emotional outbreaks, fear of oncoming insanity, hysterical fits, and her inability to render the outline of her condition a continuous narration, all pointed to the marked mental or psychic disturbances with which the patient was afflicted. The tremor of the fingers and toes has already been mentioned; there was an exaggeration of the tendon reflexes. Babinski and other abnormal reflexes were absent.

Remarks.—It was evident that here we were dealing with a case of marked thyroid toxemia in which the patient if not promptly relieved, was doomed. The mental manifestations, the extreme exophthalmos described above, endangering the eyes to the possible extent of panophthalmitis and rendering the patient extremely uncomfortable to say the least; the rapid pulse with the presence of an enlarged heart and a mitral regurgitation, which latter seemed to be losing compensation as evidenced by the edema of the legs; the poor digestive function; the rapid loss of strength and weight; all pointed to a doubtful prognosis.

Treatment

Hygienic.—The hygienic regimen given this patient was practically the same as that of Case I, with the following additions: She was instructed to rest in bed for one or two hours after breakfast and lunch, for the purpose of giving the circulatory system an opportunity to restore its compensation. All business and domestic duties were prohibited. The household attendants were informed that the children were not to disturb the patient at any time, especially during rest. After two or three months of this routine, as the patient improved, she was sent to a small country place several miles from her home, for a more complete physical and mental relaxation. She stayed there five or six weeks, during which time her improvement was very marked, and then returned home. Her domestic duties were resumed seven months after beginning of treatment, and very soon afterward she again began assisting her husband in their business.

Dietetic.—The dietetic regulations were almost identical with those given in Case I. As she was very fond of broiled steak, a small portion was permitted her once or twice a week. It was difficult to convince her of the necessity of discontinuing the use of coffee, but this was finally accomplished. As we were here contending with a very difficult gastric condition in which aversion to food, pain, tenderness, eructations of gas, and even vomiting followed the ingestion of a moderate quantity of food, it was necessary to proceed very slowly with her diet, administering treatment for her stomach as well as for the hyperthyroidism. She was especially warned against eating rapidly, and the principles of "Fletcherism" were carefully outlined to her.

Medicinal.—As the patient suffered with intermittent constipation alternating with diarrhea, it was deemed advisable mildly to stimulate the intestinal and biliary functions, and accordingly, a teaspoonful of sodium phosphate was ordered to be administered in a glassful of warm water an hour before breakfast every morning. Locally, she was given the camphor-menthol, tr. belladonna, and tr. iodine combination similar to that of Case I, to be painted lightly on the thyroid area every night. Internally, she was given the following prescription:

℞ Quinina hydrobrom. gr. iv
Lecithin gr. ii
Erythrol tetranitrat. gr. i
Ferri arsenias gr. 1/8
In capsule No. 1,
Mitte tales doses No. XXX
S.—One capsule after each meal and at bedtime.

The quinine hydrobromate was given on empirical grounds. The lecithin was given for its asserted function of nervous reconstruction; in other words, it was administered in this case for its powerful alterative effect, especially on the cerebrospinal axis. The erythrol tetranitrate was added because of its very useful influence as a peripheral vasomotor stabilizer, thus relieving the heart of an undue amount of tension and enabling it more rapidly to attain the state of compensation. In this respect this drug is more certain than sodium nitrite and more stable in its effects than nitroglycerine. The ferri arsenias was given for its obvious hematic effect. In this case, it was evident then, that unless we could at once overcome the gastrointestinal difficulties, we would lose out. Accordingly the following formula was tried:

℞ Ext. Hyoscyam. gr. 1/3
Bismuth-subcarbonat.
Mg. oxidi ponderosi āā gr. vi
M. et fiat chart. No. 1
Mitte tales doses No. XXX
S.—One powder one-half hour after meals.

The bismuth and the magnesia served to control the gastric distress incident upon the extreme hyperacidity of the stomach. The patient was instructed to take an extra powder whenever the gastric symptoms reappeared, so that she was allowed as many as five or six doses in twenty-four hours.

During the ensuing two weeks, the patient's condition, with the exception of her indigestion, was not materially improved, and she was very much discouraged. Her rheumatic pains were so severe that she was hardly able to walk. These pains were present in the elbows and knees and also throughout the chest. I decided that the supplementary use of electricity in the form of the d'Arsonval current given in the autocondensation chair would possibly help her, and administered a treatment every other day, each lasting twenty minutes. These seemed to benefit her gradually, and soon the patient's mental attitude was more optimistic.

On September 1, 1914, approximately six weeks after the beginning of treatment, her pulse was reduced to 80 per minute, circumference of neck 13¾ inches,—¼ of an inch less than before. Her nervousness was improved slightly, digestive processes very much better, sleep was more refreshing, and her weight was 105 pounds, a difference of 8 pounds. The patient at this time complained that her capsules (which contained quinine hydrobromate, lecithin, and erythrol tetranitrate) were not only too expensive, but were rather difficult to obtain, and requested that I endeavor to have some other formula suffice for the purpose. Accordingly, my next formula was the following:

℞ Quinina hydrobrom. gr. v
Ext. glandulæ suprarenalis sicca gr. ii
Ferri arsenias gr. 1/10
Ergotin gr. i
M. et fiat caps. No. 1
Mitte tales doses No. XL.
S.—One t. i. d.

It will be observed that the prescription called for 40 capsules which lasted approximately two weeks, at the end of which time her weight had not materially increased though all her subjective symptoms, excepting the exophthalmos, were slightly improved. Having had quite a series of experiences with ichthyol in persons who were underfed, I decided to try the following formula with a view to effecting a more rapid increase of body weight:

℞ Quinina hydrobrom. gr. v
Ext. glandulæ suprarenalis sicca gr. ii
Ergotin gr. i
Ferri arsenias gr. 1/10
Ichthyol gr. i
M. et fiat caps. No. 1
Mitte tales doses No. XXX
S.—One t. i. d. one hour after meals.

Ten days later, approximately ten weeks after treatment was begun, her weight was 108 pounds, and for the first time, she told me she felt well. This treatment was continued until November 10, when her weight was 111 pounds, pulse 78; the exophthalmos, although apparently as marked as ever, did not give rise to much discomfort; she was less nervous, slept better, appetite was very good, digestion practically normal.

I decided that at this point it would be well to reduce the quantity of medication, and accordingly discontinued the powder for her indigestion, telling her to take an occasional dose only when necessary and changing her quinine formula to the following:

℞ Quinina hydrobrom. gr. v.
Ferri arseninas, gr. 1/10
Ichthyol gr. i
M. et fiat caps. No. 1
Mitte tales doses No. XL.
S.—One t. i. d.

This treatment was continued until the case was discharged.

Electrotherapy.—As before intimated, she received the high frequency current in the form of autocondensation, at first every other day, later twice a week, and finally once a week. This seemed at first to have a very decided alterative effect on her nervous system, and in the course of two or three months, she found to her great delight that her rheumatic pains completely left her. In an endeavor to expedite the reduction of the size of the organ I applied the high frequency current over the thyroid gland for five or ten minutes by means of the vacuum glass electrode, just prior to each antocondensation treatment. Whether or not this assisted in the process, I am unable to affirm, but the gland gradually but surely was reduced in size and was normal when the case was discharged. Eight months after the treatment was begun, although the exophthalmos was still marked, it had materially improved. The patient however, was still obliged to protect her eyes from exposure to the air by covering them with some fabric material as she went to bed. I decided that this case could not be discharged until the eyes no longer bulged to the extent of exposure through the night, and began the use of the high frequency glass vacuum electrode applied over the closed eyes for ten or fifteen minutes twice a week. This seemed to have a most salutary influence on the exophthalmic state, for in the course of several weeks, the patient was entirely relieved of the distress of exposed conjunctivae and was able to retire without her usual protection.

At this time (June, 1915), eleven months after beginning treatment, the patient's weight was 120 pounds, heart 76, *and there was no murmur audible!* Not only had all evidences of edema disappeared many weeks before, but I found on careful examination of her heart, that it contracted to practically the normal limits.

It seems then, that in the favorable progress of events during the treatment of this patient, the restoration of cardiac compensation was due to a contraction of the myocardium, overcoming the relative insufficiency of the left ventricle, a condition with which the patient was suffering at the beginning of the treatment and which was at that time leading to loss of compensation. The patient's nutrition at this time was more than satisfactory. Her appetite was ravenous, her sleep sound and refreshing, her heart behaving naturally, her capacity for work was greater than it had been for years, and her neck was normal in appearance. There were no more tremor, hyperidrosis, gastrointestinal disturbances, nervousness, nor even rheumatic pains. In brief, the patient continually remarked that she was feeling fine, and wanted to know when she would be discharged.

On October 17, 1915 (approximately fifteen months after beginning of treatment) I discharged the patient cured. She now weighed 124 pounds (a total gain of 27 pounds), and was in every respect a strong, healthy woman. I instructed her to report to me every month or two, which she has done, and at this writing she has not been taking any treatment since her official discharge and is enjoying perfect health.

Remarks.—This was an advanced case made even more difficult of management by the presence of the rheumatic manifestations. Cases of this sort, even from the view of "operative recovery" are poor surgical risks. But from the practical viewpoint of rational nonoperative treatment, she was restored to her former health and happiness, and is 100 per cent well.

Case III.—*Mr. J. C.*, aged forty-three. Appeared in my office August 20, 1917, with a history of having been unable to work for three months because of gradual loss in weight, night sweats, nervousness, excitability with periods of melancholy alternating with hysterical outbreaks.

Family History.—Negative.

Social History.—Nothing of importance which would lead to the etiology of his condition. He is married; wife and children are well. Has no harmful habits. Is a machinist by occupation.

Past Medical History.—Nothing important. Does not remember having had any serious illness.

Present Illness.—About six months before he began to lose weight and strength, gradually. As time went on, he found himself so nervous that one month after the onset of this condition he was obliged to leave his position. His continued loss in weight and the night sweats led his family physician to diagnose his case as that of pulmonary tuberculosis. The treatment for the latter being unsuccessful, he consulted another physician who made a diagnosis of nervous dyspepsia. Finding that he was going from bad to worse he consulted another doctor who diagnosed his case as a "nervous breakdown." His condition, however, reached the point where he was obliged to spend most of his time in bed. When he came to me, three months after he began ailing, I discovered that he was a case of hyperthyroidism in the early stage, with marked preponderance of the nervous manifestations. The patient had lost 20 pounds in weight during his illness; there was frequent nocturnal micturition, sweating almost every night, and a strong tendency toward excessive sentimentality which would lead him to periods of sobbing.

Physical Examination.—Patient was a fairly well-nourished man weighing 132½ pounds. Facies somewhat anxious, and there was considerable restlessness as he appeared before me in the office. *Skin*: somewhat plethoric in appearance; texture rather moist; dermographia obtainable; no scars or edema. *Head and Scalp*: negative. *Glands*: lymphatic glands practically normal. *Eyes*: moderate exophthalmos which became more marked when concentration of attention was attempted. In this relation he told me that for some time past his friends had told his wife that he had an uncanny, frightened and unnatural look in his eyes, especially when talking. Stellwag's, Dalrymple's, Moebius' and Von Graefe's signs were obtainable. Pupils reacted to light and accommodation. Extraocular movements were good. *Mucous Membranes*: conjunctiva, nose, throat, and gums slightly congested. *Lips*: somewhat bluish. Tongue a light whitish coat; protruded without a tremor. *Neck*: throbbing of the carotids and slight pulsation of the jugulars. The thyroid gland presented a slight symmetrical enlargement, only noticeable on close inspection and palpation. In fact, the patient during the entire period of his illness paid very little attention to the thyroid hypertrophy, and only when I spoke of it did he remark that he, too, thought his neck was slightly larger than usual. Auscultation over the thyroid area revealed a soft, musical, systolic hum. *Chest*: practically normal on inspection, palpation, percussion, and auscultation, excepting that there was a respiratory expansion of but 2½ inches. The apical impulse could be seen in the fifth left interspace slightly within the midclavicular line and was somewhat impetuous in character. There were no murmurs discernible, but the heart sounds were somewhat weaker than normal. Pulse 82 per minute; regular, rhythmical, poor volume and low tension. *Abdomen*: slight tenderness of epigrastric area. *Limbs*: nothing abnormal excepting that the outstretched fingers and toes presented a fine tremor. *Nervous System*: in addition to the fine tremor mentioned there was a moderate increase in the tendon reflexes. Although the patient seemed to possess average intelligence, he was prone to morbid ideas about himself, to the extent of melancholia at times.

Remarks.—In all fairness to the doctors whom this patient consulted, it must be said that this was one of the elusive cases occasionally encountered. The exophthalmos was not at all marked excepting during conversation and active attention, and was therefore overlooked. The tremor was not sought for; the increased heart rate was not marked enough to excite suspicion and was probably attributed to nervousness on the one hand or as a constituent of tuberculosis on the other. The marked loss in weight and strength and the sweating served to emphasize the probability of tuberculosis. All these, plus the absence of a markedly enlarged thyroid, rendered the diagnosis rather a difficult one.

The diagnosis of Graves' disease was here made by the absence of pulmonary phenomena and other infectious processes, the absence of a definite syndrome characteristic of nervous indigestion and the presence of moderate tachycardia, exophthalmos, thyroid hypertrophy, tremor, change in disposition especially emotionalism, and last, but not least, *the rapid improvement under treatment for Graves' disease.*

Treatment

Hygienic.—The hygienic regulations given this patient were those indicated in the previous chapter. He was instructed not to resume work until further orders. He and the family were advised to avoid all factors which would lead to his mental and physical excitation, and the importance of complete tranquility of body and mind was insisted upon.

Dietetic.—The dietetic regulations were those suggested in the previous chapter. Animal foods were reduced to a minimum, and this was compensated for by an increase in the quantity of dairy products and cereals. Tea, coffee, cocoa, tobacco, alcoholic beverages and the condiments of the table were strictly prohibited. He was advised gradually to increase the quantity of food as the capacity of his digestion increased.

Medicinal.—As there was slight constipation, a teaspoonful of sodium phosphate in a glassful of hot water an hour before breakfast daily, was ordered. Locally the following ointment was prescribed:

℞ Ungt. hydrarg. oxidi Rub. ʒ i
Lanolini ℥ ii
A small portion to be rubbed into the thyroid gland every night.

Also the following was prescribed:

℞ Quinina hydrobrom. gr. v
Spartain sulph. gr. 1/2
Ext. belladonnae gr. 1/4
Ferri arsenias gr. 1/10
M. et fiat capsule No. 1
Mitte No. XXX.
S.—One t. i. d.

In addition to this medicinal treatment, he was given an autocondensation treatment three times a week.

This system of therapeutics was persisted in for three months, at which time the patient felt entirely normal. The exophthalmos was almost gone, the pulse was 70 per minute, tremor had disappeared, appetite was ravenous, sleep and nervous system were entirely normal, and there was an increase of 20 pounds in weight. This patient, who had been informed by one physician that he was incurable and would probably live but six months, was now a cheerful, robust, optimistic man, ready to resume his work.

At this juncture he was informed of the advisability of abstaining from work for three months longer. The prescription ointment was discontinued, and he was given quinine hydrobromate in 5 gr. capsules three times a day, and electrical treatments once a week. At the end of the second three months of this treatment, or six months after treatment was started, the patient weighed 158 pounds, which was more than he had ever weighed in his life, and aside from an almost imperceptible degree of exophthalmos, he appeared a perfect specimen of manhood. He was informed that the slightly persistent exophthalmos would disappear within six months or a year, and he was ordered back to work.

At this writing the exophthalmos has entirely gone, and the man is enjoying perfect health.

Case IV.*—Mrs. M. J., white, aged 55, a rather stout, plethoric looking woman, appeared in my office March 22, 1918, complaining of nervousness, insomnia, irritability, palpitation, indigestion, constipation and marked sweating.

Family History.—Negative.

Social History.—Indulged moderately in tea, coffee and alcoholic beverages. Married twenty-four years; two children; no miscarriages; menstrual history normal; menopause five months previous to this time.

Past Medical History.—Negative, excepting that, with the birth of her youngest son, eighteen years before, she developed an enlargement of the neck which gradually increased in size, until at the present time the mass is quite large.

Present Illness.—About one year before, patient began to complain of the above-mentioned symptoms for which she applied for treatment. The nervousness, insomnia, palpitation, sweating and weakness were gradually becoming so marked that she was unable to perform her household duties.

Physical Examination.—Patient was well nourished, weight 170 pounds, rather nervous-looking, and presented a medium sized goiter. *Skin*: moist and erythematous; dermographia obtainable. *Lymphatic Glands, Head and Scalp*: negative. *Eyes*: slight exophthalmos; Dalrymple's, Von Graefe's, Stellwag's, and Moebius' signs not marked; reaction to light and accommodation normal. *Mucous Membranes*: somewhat congested. *Lips*: dry. *Gums and Teeth*: in poor condition. *Tongue*: slightly coated and tremulous. *Throat*: chronically congested including tonsils, which latter presented several folliculi. *Neck*: a goiter which was the size of a large orange located in the median line. It was somewhat doughy to the touch, but no tenderness was elicited on deep palpation. The greatest circumference of the neck was 17¼ inches; superficial vessels slightly more prominent than normal; palpation did not reveal thrill; and on auscultation no murmur over neck was discoverable. *Chest*: negative, excepting that the heart area presented evidences of moderate hypertrophy with an increased force and frequency of the systolic impulse. *Pulse*: full, regular, rhythmical, 100 per minute. Moderate fibrosis present. Systolic blood pressure 155 mm.

---

*This case and those following were published in an article entitled, "The Nonoperative Treatment of Toxic Goiter" (International Clinics, Vol. XXIV, Series 29).

Remarks.—It was evident that here we were dealing with a case of oldstanding simple or nontoxic goiter (induced by pregnancy) which at this time was undergoing toxic changes. In other words, there was a gradual development of secondary hyperthyroidism, giving us what is commonly termed the "Basedowified" goiter. I informed the patient that in all likelihood the goiter would not disappear without operation, but that we might be able to relieve her of the symptoms of which she was complaining, after which she might undergo operation for the removal of the goiter if she should so desire.

Treatment

The regulation dietetic and hygienic instructions as outlined in the aforementioned cases were given this patient.

Medicinal.—Locally, the following ointment was prescribed:

℞ Ungt. Hydrarg. Oxidi Rubri ʒ iii
Lanolini q. s. ℥ iii
S.—A small portion to be rubbed into goiter area every night, after which some of it is to be lightly applied over the neck and a soft cloth wound around for the night.

The following was prescribed for internal administration:

℞ Quinina hydrobrom. gr. v
Sodii nitrit. gr. i
Ext. hyoscyamus gr. 1/3
Aloini gr. 1/10
Veronal gr. ii
In caps.
S.—One t. i. d.

As a supplementary measure, the high frequency (d'Arsonval) current was given her in the autocondensation chair for that purpose, twice a week. This latter procedure was employed with a view to assisting the reduction of her blood pressure.

After four months of the above treatment, the patient was cured of her symptoms; the blood pressure remained below 150, and her heart rate stayed between 70 and 76.

At this writing the patient's condition, so far as her toxic symptoms are concerned, is normal, the circumference of her neck is reduced to 16½ inches, a diminution of ¾ inch.

In this case we were able to overcome the secondary toxic symptoms superimposed upon the simple goiter by non-surgical measures, but the goiter itself will have to be removed by the surgeon, else it may again assume a toxic picture at some future time.

Case V.—Señora T. L. deN. deT., residence, San Luis Potosi, Mexico.

On February 5, 1913, a neat-looking Mexican called on me and asked whether I would undertake to relieve his wife of the symptoms of hyperthroidism. The señora was at their home at San Luis Potosi. I told him that it was not my practice to administer the "absent treatment," but he assured me that he could fully describe her condition in every detail, and that if I but undertook to prescribe according to his description now, he would within the next four or five months bring her along to my office. He told me that he could not leave Philadelphia at that time, as he was actively engaged in some enterprise which meant his continued application for the next three months. As the man seemed very intelligent and thoroughly conversant with the subject of hyperthyroidism, having studied his wife's condition carefully, I decided to accept the case temporarily, pending her visit to Philadelphia. In brief, the following is the description forwarded for my scrutiny:

Mrs. T. L. deN. deT. was thirty-five years old, medium height, housewife; had been in perfect health until about three years before, when, through some incident connected with the factional warfare in Mexico, she was badly frightened. From that time on dated her present illness.

Chief Complaints.—Marked loss in weight, palpitation, extreme nervousness, insomnia, great weakness, and occasional diarrhea.

Family History.—As far as could be determined, family history was negative.

Social History.—Married twelve years, had four children: oldest child eleven, the youngest two years old. The last two births were accompanied by hemorrhages. No miscarriages. Personal habits of patient were good, as far as could be determined.

Past Medical History.—Although nothing definite could be obtained, it seemed that the patient had been in perfect health up to the time of present illness.

Present Illness.—Dated back three years when patient was badly frightened. A few weeks later, she began to notice swelling of the neck; at the same time, there were gradually increasing nervousness and insomnia, bulging of the eyes, frequent hysterical attacks, marked anemia, poor digestion, occasional troublesome diarrhea. Her appetite became progressively poorer until it left her completely, and there was a very rapid loss in weight and strength. There was no subjective sense of cardiac discomfort until she had been ill for six months, when palpitation, increasing in frequency and intensity, became a marked feature. Her husband took her to local physicians who could not offer relief, suggesting operative measures. He then took her to Mexico City, with similar results. Finally, he crossed the border with her and found himself consulting American physicians in California, Arizona, Texas, and New Mexico, but with no material improvement. After twelve or fourteen months' effort to relieve her, he gave up the idea of doctoring and decided to do all he could for her himself. He proceeded to invest in medical books dealing with the subject. However, she seemed to be going from bad to worse, now weighing but 100 pounds, having lost approximately 80 pounds during the past three years. He stated that he had found his way into my office on the advice of a medical student of one of the classes which I was instructing at that time at the Medico-Chirurgical College.

Physical Signs.—Of course, I could not get a record of physical signs, but so far as I could determine from the history given by the patient's husband, we were dealing with a typical case of exophthalmic goiter. Here were an enlarged thyroid, tachycardia (which the husband stated averaged 140 per minute), exophthalmos, and probably tremor (although the husband could not give me definite information of same). There were emotional outbreaks in the form of hysterical attacks, persistent insomnia, digestive disturbances, diarrhea, marked loss in weight and very marked wasting of the body.

Treatment

Having outlined the course of hygienic and dietetic regulations, I wrote out for him the following prescriptions:

℞ Quinina hydrobrom. gr. v
Ext. belladonnæ gr. 1/8
Ext. glandulæ suprarenalis gr. ii
Ferri Arsenias gr. 1/12
M. et fiat caps. No. 1; mitte tales doses No. cclxx.
S.—One t. i. d. p. c.

℞ Camphor-Menthol ʒ i
Tr. belladonnæ ʒ iv
Tr. iodi q. s. ad. ℥ i
S.—Paint lightly over thyroid gland once daily.

These prescriptions were dispensed in Philadelphia and sent off to the patient. The patient's husband at the same time sent her a long, carefully written letter, translating the hygienic and dietetic regulations.

On his inquiry regarding my prognosis, I told him that the favorable progress of this case was hampered by the duration of the illness and by my inability to see her, but I thought that it was within the realms of possibility materially to improve her in this fashion during the next twelve months, if orders were faithfully obeyed. He assured me that his wife and he would do all they could to cooperate with me toward attaining the desired result. Three months later he called on me again and reported that his wife was at least 50 per cent improved. She was so much better that she felt almost well and had rapidly gained in weight. Having promised that he would bring her over to Philadelphia within the next three months, I merely duplicated the above prescriptions which were again dispensed in Philadelphia and forwarded to Mexico.

Two months later he appeared in my office again, asking for duplicates of the prescriptions, informing me that it would be impossible for a long time to bring his wife (to Philadelphia, and that she had written to him to effect that she "would fool the doctor; that it would take a year to cure her, but that she expected to be as as she had been previous to her illness, in another m(or two." I duplicated the prescriptions; he left me wi most gracious *adios,* and I have not heard from him si

Was it that the extreme elation of being so promptly lieved so overwhelmed them that they excluded the w from their mental horizon, or was it because of war co tions and possibly a serious attack on the locality by a r military faction? Of course, I do not know, for I did receive any response to the several letters of inquiry w I sent during the ensuing year. Judging from the al history and the favorable progress of events, there is ery reason to believe that this case was cured comple or would have been entirely cured in the absence of del rious unforeseen circumstances. According to newspa reports at that time, San Luis Potosi, where they resi was subject to frequent bombardments and street figh by the then equally matched military rivals.

CASE V.—Mrs. L. G., white, age thirty-four, weight pounds. Sent to me February 2, 1915, complaining of n ousness, cardiac palpitation and very troublesome indi tion. During the past six months she had noticed that eyes had been protruding forward and that she persp profusely on the slightest provocation. She also c plained of considerable loss in weight, marked weak and shortness of breath.

Family History.—Unimportant.

Social History.—No points of interest. Married years; had two healthy children; no miscarriages. Did own housework, but did not overwork.

Menstrual History.—Normal.

Past Medical History.—Had the usual diseases of ch hood, no other diseases, excepting that during past sev years she had been suffering with indigestion which so marked at times as to cause her to fear to eat.

also troubled at times with constipation alternating with diarrhea.

Present Illness.—About two years before, patient became very nervous. This nervousness was characterized by irritability of temperament, restless sleep, fear of impending calamity, fright on the slightest provocation and occasional exacerbations of emotionalism, almost amounting to, but not reaching, typical spells of hysteria. About six months later she began to notice that her neck was assuming a greater circumference, and there was a tendency to a slight, irritating, nonproductive cough which seemed to issue from the vocal cords. Coincident with this, she noticed that her eyes had an unusual stare which was gradually becoming worse. About a year before this time she had become troubled with palpitation which was especially marked on retiring and also during slight physical or mental exertion, at which time shortness of breath was very evident. The indigestion which she had had for some time was now becoming worse, and being unable to eat, she was losing very much in weight. There was at this time anorexia, a sense of fullness in the stomach immediately after beginning a meal, flatulence and eructations of gas and sour material, occasional vomiting, tenderness over the pit of the stomach, and often attacks of sharp pain and a feeling at times of "heart-burn," which caused her to take large quantities of sodium bicarbonate for relief. Constipation was also markedly increased, so that if she were not to take a cathartic, three or four days would elapse without a bowel movement. Her nervousness was very acute. She could hardly sleep because of the mind wandering into morbid paths and also because of excessive sweats which occurred almost nightly. Thus, when she arose in the morning, she was more tired and languid than on retiring. Her sense of weakness was such that she could hardly walk a half mile without resting. She complained of dull aches and pains in her lower limbs and a feeling as though the flesh were beaten. During the preceding six months, she claimed she had lost about 15 pounds in weight.

Physical Examination.—Patient was a poorly nourished woman; appeared anxious and nervous as she was being examined. *Skin*: Somewhat dusky, soft and moist; dermographia obtainable; superficial veins more prominent than normal; especially those about the neck and thyroid gland.

No scars or edema. *Lymphatic Glands*: practically normal. *Head and Scalp*: normal, except that the hair was becoming gray and scarce. *Eyes*: typical exophthalmos bilateral; Stellwag's, Dalrymple's, Moebius' and von Graefe's signs present in both eyes. Reaction to light and accommodation practically normal. Extraocular movements slower than normal. *Conjunctiva*: slight congestion and epiphora. *Nose*: practically normal. *Lips*: somewhat dry, otherwise normal. *Gums*: paler than normal. *Teeth*: evidences of careful dentistry. *Tongue*: protruded with a tremor, slightly coated. *Throat*: slight congestion; tonsils somewhat prominent but apparently healthy; pharynx slightly cyanotic. *Neck*: fourteen and one-half inches at greatest circumference. There was a thickening of the thyroid gland which was soft and diffuse, corresponding almost completely to the horseshoe shape of the thyroid, *i.e.*, the isthmus and both horns were equally and continuously hypertrophied. Palpation confirmed inspection, deep palpation eliciting tenderness. Auscultation revealed a soft, musical, systolic bruit over all parts of the thyroid. *Chest*: on inspection the anteroposterior diameter of upper half was diminished. Ribs, clavicles, and scapulæ prominent. Respiratory expansion 2 inches. The apical beat was seen in the fifth left interspace in the midclavicular line; it was somewhat diffuse, extending over a radius the size of a silver dollar. Tactile fremitus universally increased. Pulse 120 per minute, weak, soft, low tension, compressible although regular and rhythmical. Percussion revealed a slight cardiac hypertrophy, the left border of the heart extending to the midclavicular line. Pulmonary resonance practically normal. Heart sounds were practically normal except that the first apical sound was somewhat weak. The breath sounds were universally exaggerated. Vocal fremitus slightly increased over both apices. *Abdomen*: practically normal. *Limbs*: emaciated. Superficial veins more prominent than normal. Typical tremor of outstretched fingers, less marked of the toes. *Nervous System*: occasional choreiform twitch of various parts of the body. The patient when made to concentrate her mind upon a question was capable of coherence and continuity of thought. The reflexes were exaggerated; Babinski's sign absent; typical tremor present.

Treatment

Hygienic.—The hygienic regime was that indicated in the previous chapter. A rest of an hour or two in bed after each meal was strongly insisted upon. All mental and physical excitation was warned against. A daily lukewarm tub bath at bed time was advised.

Dietetic.—The dietetic advice was that outlined in the foregoing cases. With the exception of an occasional portion of broiled or stewed white meat of chicken, the diet was strictly nonflesh in character. She was urged to eat slowly.

Medicinal.—The following was prescribed locally:

℞ Ungt. potasii iodidi ℥ i
S.—A small portion the size of a bean to be massaged into the thyroid area until the skin is dry, every night.

The following capsule was given:

℞ Quinina hydrobrom. gr. v
Ferri arsenias gr. 1/10
Aloini gr. 1/8
In caps. No. 1
Mitte tales doses No. XXX
S.—One t. i. d. p. c.

Also, a tablespoonful of milk of magnesia was ordered to be taken a half hour after each meal. This was given for the purpose of neutralizing the excess of acidity accompanying the nervous dyspepsia. Electrical treatments every other day were given from the beginning. This was administered in the form of the d'Arsonval current in the autocondensation chair. Ten days later, patient reported progress; subjective cardiac symptoms were less marked, pulse 104, sleep somewhat better, 2 pounds increase in weight, digestion improved. The above capsule was repeated with the addition of 1 gr. of veronal to the dose. During the next ten days, the patient's nerves were so markedly improved that, when she appeared in my office on February 22, she made no mention of nervousness. Sleep was almost normal, heart improved, pulse 100, hyperidrosis lessened, gestion improved.

This improvement continued gradually under the s treatment, with an occasional slight recurrence of the i gestion until May 5, 1915 (three months later) when weight was 118, pulse 86, digestion almost normal, and t was a universal improvement in well-being. At this ti I prescribed again, instructing her to call at the usual ti It seems that the patient imagined herself entirely wel this point, for I did not see her again until February 1918, when she appeared in my office, asking to be relie of indigestion. There were no evidences of exophthal goiter, and she appeared a perfectly normal woman in ery respect, subjectively and objectively.

Remarks.—It seems that in this case, the beginning improvement through remedial measures started the p esses of the bodily forces in efforts at a reestablishmen the normal relationship between the various internal se tions. That this is probably true, is emphasized by fact that some cases of hyperthyroidism become well s taneously.

Case VII.—Mrs. M. A., age fifty, was sent to me on O ber 11, 1916, suffering with enlarged thyroid, nervousn palpitation, insomnia.

Chief Complaints.—Swelling of the neck, spells of n ousness, inability to sleep, poor vision, marked indigest palpitation.

Family History.—Her mother and aunt had goiter, nature of which she was unable to describe.

Social History.—Married twenty-five years; no child No history of venereal disease obtainable. Habits drank one cup of coffee a day and took a moderate q tity of meat and condiments. Performed her own ho work.

Menstrual History.—Presented nothing abnormal. M opause occurred eight years ago and was complete and eventful.

Past Medical History.—Did not remember having any of the diseases of childhood. Had an attack of a articular rheumatism four years previous to this time, from which she had not fully recovered, as evidenced by the presence of enlarged, somewhat tender joints of the fingers and toes. She had been suffering with varying degrees of indigestion for several years.

Present Illness.—About two years before, patient began to notice an increase in the circumference of the neck, which made it difficult for her to fasten high-necked clothes which formerly had fitted well. She also experienced occasional choking sensations which at times culminated in nonproductive cough apparently caused by some pressure on the vocal cords. At the same time, she began to complain of nervousness and insomnia. She stated, too, that her vision began to fail her from that time, and that the indigestion became very much worse. There was gradual diminution of appetite and progressive loss in weight, until now she was approximately 12 pounds below her usual weight. She was suffering with a continuous sense of fatigue in the lower limbs. Bowels were normal.

Physical Examination.—Patient was a fairly well-nourished woman of fifty. She appeared entirely rational, answering all questions promptly and to the point. *Skin*: normal in texture and moisture; there was slight dilatation of superficial veins. Dermographia elicited.

Head and Scalp: negative. *Eyes*: slight exophthalmos; von Graefe's, Stellwag's, Dalrymple's, and Moebius' signs not marked; a moderate degree of presbyopia, rendering her unable to sew or read without the aid of the proper glasses. *Conjunctiva*: slightly congested. *Nose*: normal. *Lips*: slightly paler than normal. *Gums*: slight recession of lower gums and moderate pyorrhea, necessitating correction by dentist. *Tongue*: normal. *Throat*: slight degree of chronic congestion, not unlike the rheumatic throats often described in textbooks. Tonsils were somewhat prominent. *Neck*: moderate prominence of thyroid gland, more marked over the isthmus than the horns. The enlargement was soft and diffuse, the neck measuring 14 inches at greatest circumference. Palpation negative. No tenderness elicited. Auscultation presented a soft systolic murmur over prominent part of thyroid. *Chest*: nothing abnormal. Pulse rate 84 per minute of good volume and tension, regular and rhythmical. *Abdomen*: practically nor *Limbs*: slight dilatation of superficial veins. No ed Enlarged joints of fingers and toes, indicating rheun deposits. *Nervous system*: very fine tremor of outstret fingers. Otherwise, the nervous system presented not abnormal so far as could be ascertained.

Remarks.—Here we were dealing with a case of e form of hyperthyroidism, in which the disease had not beyond the incipient stage so far as clinical symptoms concerned.

Treatment

Hygienic.—Patient was not given many precise hygi directions, her environments required but little correc and her habits were fairly good. She was instructed to an afternoon nap daily, or at least a rest in bed. Mode exercise was not interdicted. She was warned against due physical or mental excitation and was advised to a herself of a moderate quantity of healthful recreatio the form of outdoor games, attendance at theatre par lectures, etc. She was ordered to have her eyes refra and teeth attended to without delay.

Dietetic.—Because of poor digestion, the dietetic r lations were modified by occasional variations in accord with the exigencies of the digestive functions. The di tive difficulty here appeared to be that of the ordinary t of nervous dyspepsia which was promptly controlled by following formula:

℞ Bismuth subnitrat. ʒ iii
Tr. hyoscyamus ʒ iv
Aq. sodæ menthæ q. s. ad. ℥ vi
S.—Shake well; teaspoonful in water before and after mea

The dietary regime was mainly nonflesh in charac excepting that a small portion of tender steak or white m of chicken was allowed two or three times a week. In ot respects, the dietary instructions were similar to that lined in the previous cases.

Medicinal.—The following was given locally:

℞ Menthol
Camphor āā gr. v
Tr. belladonnæ
Tr. iodi āā ʒ ss.
S.—Paint lightly over goiter every night or every other night, depending on the toleration of the skin.

The following capsule was prescribed:

℞ Quinina hydrobrom. gr. v.
Veronal
Ergotin āā gr. i
M. et fiat caps. No. 1
Mitte tales doses No. XXX
S.—One t. i. d. p. c.

In addition to this treatment, the patient's thyroid gland was treated by the application of the high frequency current in the form of the vacuum glass electrode for fifteen minutes twice a week.

As the patient resided in a distant town and her financial resources were meager, she was able to call only once every two or three weeks after the second week of treatment. I did not object to this infrequency of observation as she was very cooperative, and her condition was not urgent. Four weeks later the patient's pulse was 76, the choking sensations and the occasional dry cough had disappeared. Her nervous system and sleep were very much improved, and the indigestion was gone.

After the fourth month of treatment, the patient was restored to her usual weight and health, and the circumference of her neck was reduced by 3/4 inch, which made it appear normal. At this point the patient begged to be permitted to discontinue treatment because of financial difficulties. She was accordingly discharged with instruction to report to me in case of relapse. At this writing I have heard from her several times, informing me that she is enjoying the best of health.

CASE VIII.—Miss L. B., age twenty-four, weight 125 pounds, appeared in my office for treatment November 29, 1917, complaining of large neck, choking sensations, loss of weight and strength, nervousness, insomnia, palpitation and excessive sweating.

Family History.—This was negative, excepting that a younger sister was suffering with goiter and nervous dyspepsia. Patient stated that her sister's condition was improving, without treatment.

Social History.—Unimportant. Habits good; had been working as mill hand for some years.

Menstrual History.—Negative.

Past Medical History.—Had most of the diseases of childhood; no diseases since; had been nervous for several years.

Present Illness.—About four years before, a few weeks after a fright, she became more nervous than ever, and at the same time noticed a swelling of the front of her neck. Loss in weight and palpitation were soon quite evident, so that she sought medical advice. The doctor treated her for "nervousness" and "indigestion" for some months, but on the appearance of well-marked exophthalmos the diagnosis of Graves' disease was made. At this time she became troubled with incontrollable irritability of temper, drenching night sweats, sleeplessness, nausea, great weakness in the limbs, diarrhea, and polyuria. Operation was suggested, but patient would not entertain the thought and continued to be treated by medicinal measures. Her condition becoming worse at this time (one year after the onset of the disease), she was sent to a hospital for the rest cure, where, after three months' treatment, her weight, which had been reduced to 100 pounds, was increased to 135 pounds, with a concomitant improvement in subjective symptoms. However, the palpitation, exophthalmos, and goiter were unimproved, and she sought treatment elsewhere. For another year she went from one doctor to another and from clinic to clinic where she received no encouragement but the remark that the goiter had better be operated on. Firm in her determination not to yield to operation, she decided to stop doctoring. For a year or more she stayed home and rested, feeling fairly comfortable. After this time all her symptoms began to reassert themselves with greater intensity than ever, so that she decided once more to seek medical aid. When she appeared in my office she presented the following physical signs:

Physical Signs.—Patient was a poorly nourished woman, very nervous, presenting an unusually large symmetrical thyroid enlargement and extreme exophthalmos. *Skin*: soft and moist with occasional erythematous areas distributed over the face, neck, and chest. Superficial veins over thyroid gland were prominent. *Lymphatic glands*: more palpable than normal. *Head and Scalp*: negative. *Eyes*: extreme exophthalmos; sclera and conjunctiva present enlargement of superficial vessels due to chronic congestion. Excessive dryness of the eyes was troublesome to the patient, and she complained of a continuous ache in the eyeballs. Stellwag's, Dalrymple's, Moebius' and von Graefe's signs marked. Reaction to light and accommodation, and extraocular movements were sluggish. *Nose*: normal. *Lips*: pale and dry. *Gums and Teeth*: negative. *Tongue*: protruded with a tremor and was slightly coated. *Throat*: congested. *Tonsils*: enlarged with some evidences of having been subject to attacks of inflammation. *Neck*: fifteen and one-half inches at greatest circumference. The thyroid gland was unusually enlarged for a case of hyperthyroidism. The swelling was soft, symmetrical, somewhat more marked over the right lobe than the left. On palpation, a systolic thrill could be felt over the thyroid, and on auscultation, a harsh, blowing murmur was heard, more marked during systole than diastole. Deep palpation, especially with the patient's neck extended, elicited tenderness. *Chest*: normal in type but somewhat emaciated; respiratory expansion 2 inches; apex beat not visible. *Palpation*: negative, excepting over cardiac apex where the systolic impulse was somewhat diffuse to the palpating fingers. Percussion over the lungs negative; heart enlarged, apex extending to sixth interspace in midclavicular line. Auscultation of lungs negative; first apical sound of heart somewhat weaker than normal and prolonged, but no distinct murmur audible. Second sound rather weak; other heart sounds practically negative excepting that they are weaker than normal. *Pulse*: 100 per minute; somewhat small and thin; poor volume and tension. *Abdomen and Limbs*: normal. *Reflexes*: somewhat exaggerated. There was a typical fine tremor of outstretched fingers and toes.

Remarks.—This case is interesting in that the heart was not materially damaged during the rather protracted siege of hyperthyroidism. The most marked symptom was the exophthalmos, which in this case threatened to lead to corneal ulceration.

Treatment

In detailing to me her social history, patient remarked that she had been engaged to be married for several months prior to the onset of this illness, but that her present condition was a barrier to a happy union. In accordance with my deductions based upon this information, I suggested to her that a diminution in the number of meetings with her fiancé to once every week or two and the keeping of early hours were important conditions to be fulfilled if we were to look for prompt results in treatment. Subsequent revelations proved this advice to be of extreme importance, for excessive "spooning" with consequent rousing of the emotions must have had an etiologic bearing upon her condition.

Hygienic.—Patient was ordered to discontinue her vocation and avail herself of a maximum of fresh air and rest. Although the complete rest cure was not ordered, she was instructed to lie down for two hours after breakfast and luncheon and to rest at least eight hours at night. She was warned against any undue physical and mental exertion; attendance at moving-picture plays and the reading of newspapers were interdicted. She was advised to read literature of a light, humorous vein and to attend an occasional interesting lecture or musicale. A lukewarm bath at bedtime each day, was ordered. The parents were instructed with regard to complete cooperation in the treatment, and they were especially advised so to govern the household as to render the patient's environments as tranquil as possible.

Dietetic.—The regime was practically similar to that of the foregoing cases.

Medicinal.—Locally, the following ointment was prescribed:

℞ Ungt. hydrarg. oxidi rubri ʒ ii
Lanolini ℥ ii
M. et fiat ungt.

S.—A portion the size of a bean to be rubbed over the goiter area until absorbed, every night, then a small quantity to be smeared lightly over the goiter, and neck wound around with a cloth which is removed in the morning.

Patient was advised to take a teaspoonful of sodium phosphate in a glass of hot water one hour before breakfast, in case of constipation.

In addition, the following capsule was prescribed:

℞ Quinina hydrobrom. gr. v
Ferri arsenias gr. 1/12
Ergotin gr. i
In caps. No. 1.
S.—One t. i. d., p. c.

This treatment was supplemented with a ten minutes' application of a high frequency current over the thyroid gland through a glass vacuum electrode, three times a week. Two weeks later, the patient felt markedly improved, having gained 6½ pounds. Treatment was continued in the same fashion for three months, at the end of which time the heart rate was 80, all subjective symptoms had subsided, and she weighed 142 pounds,—a gain of 17 pounds. The exophthalmos, however, was still very marked, and there was considerable smarting of the eyes. At this point the aforementioned capsules were ordered to be taken four times a day instead of three, electricity over thyroid was discontinued, but instead a binocular glass vacuum electrode with high frequency current was applied over the eyes twice a week for ten minutes each time. At the end of the ensuing three months (six months after the beginning of treatment), the exophthalmos was but slightly marked, the thyroid was almost normal in size, the pulse 70 to 76 per minute, sleep was perfectly normal and refreshing, and in every possible respect the patient felt perfectly well and weighed 148 pounds, a gain of 23 pounds,—more than she had ever weighed in her life. A visit from her fiancé to my office revealed the fact that they were desirous of being married as soon as I would give the word. I felt that this would eliminate the strain incident to engaged life, and in v of the fact that her condition was entirely satisfactor gave my consent. The following month they were marr

The patient continued under my observation two or tl times a month with practically the same treatment, anc the end of the ninth month of treatment she was dischar cured. At this writing, having gone through an unev ful pregnancy, she was delivered of a fine, nine-pound b girl. Parturition was accompanied by profuse hemorrh which was finally controlled by packing of the uterus. mentioned elsewhere in this work, these patients, beca of diminished coagulability of the blood, are prone to cessive bleeding somewhat similar to subjects of he philia. Recovery was complete, and mother and b were entirely normal. It should here be noted that this tient was taking 20 gr. of quinine hydrobromate each d with no deleterious effects on the gravid uterus. The tient's condition at the present time is such that there no evidences of a former severe four years' siege of hy thyroidism.

In the treatment of exophthalmic goiter, *individualizat* is of inestimable importance. Measures which in one stance may appear very useful, may in another patient useless or even harmful, so that a brief period of experim tation may be necessary in order to discover exactly w regime is best adapted to the individual.

Rest, physical and mental, must characterize all tre ment instituted in this disease. There must be a compl harmony of the bodily and mental faculties, and there m be harmonization of the body with the mind and vice ve Having secured this harmonization among the struct and functions of the patient, we must further aim to sec the adaptation of this harmonized individual to external vironments and circumstances. No matter how successf how ingenious, how skillfully a mode of treatment might pear to be, a condition of internal or external disharmc or discord will render the treatment futile.

CHAPTER XII

CONCLUSIONS ON THE TREATMENT OF EXOPHTHALMIC GOITER

Exophthalmic goiter does not come within the realm of surgery. Surgery has for its purpose the alteration or removal of an offending portion of the anatomy, a portion which has become diseased, and the removal of which will restore health and happiness to the sufferer. Appendectomy, herniotomy, tonsillectomy, prostatectomy, hysterectomy, and gastroenterostomy are examples of perfect surgery, and the author frankly admits the advisability of the surgical removal of simple (nontoxic) goiters of moderate size. In each instance the condition is strictly *local* and *local* relief means cure. In each instance the systemic sufferings are but reflexes resulting from *local* irritation, which quickly disappear on the removal of the *local* cause. Not so with exophthalmic goiter.

Surgeons who spend much time in thyroid work have frequently offered in support of their views the analogy of the hyperactive gland as being as urgent a surgical condition as an inflamed appendix. Why remove a diseased appendix, they argue, and hesitate to remove a diseased thyroid? These men fail to observe (1) that appendicitis is a local disease while hyperthyroidism has a widespread etiology, symptomatology, and physiologic relationship; (2) that the appendix is a vestigeal organ, while the thyroid is a vital organ and must not be tampered with; (3) that the appendix, in appendicitis, is the seat of germ activity, while the hyperactive thyroid is not infected; (4) that operative removal of the appendix renders the patient well and healthier than ever, while the total removal of the thyroid means a slow death from cachexia strumipriva, and partial removal does not cure the patient, to say the least.

It has been observed by keen clinicians that gastrointestinal disease, disturbances in the genital organs, tonsillar and nasal affections, disturbances in the function of the suprarenal glands, in brief, a disturbed structural and physiologic balance of almost any organ in the body, is prone to act as a predisposing or exciting cause of hyperthyroidism. Is it consistent, then, to attack the thyroid as a therapeutic measure? Again, many instances of established hyperthyroidism, especially the *fruste* form, are somewhat atypical in manifestations, presenting evidences of an alternating hypo- and hyperthyroidism or a peculiar combination of the two at the same time. In a case of this sort, the most daring surgeon must pause for lack of determination to operate, through the intervention of his conscience.

In the presence of such confusing etiologic theories, conflicting pathologic evidences and profound systemic changes especially referable to the circulation, the nervous system, and the metabolic balance, as evidenced by the progressive loss in weight and strength, does it not seem inconsistent to place the entire blame on the thyroid gland and to proceed surgically on the assumption that the removal of this gland spells cure, *i.e.*, a restoration of the utility and happiness of the patient? It is admitted that the Basedow syndrome could be produced in animals and in human beings by the administration of excessive doses of thyroid substance. It is therefore conceded that most of the symptoms met with in exophthalmic goiter are produced by the presence of an excessive quantity of thyroid substance surcharging the blood, which is manufactured by the patient's thyroid gland. But whether the gland is primarily the cause and all the other manifestations are results of thyroid intoxication, or, on the other hand, whether the thyroid hyperactivity is really secondary to some other cause, is the question which both surgeons and internists must decide, in view of the fact that the knife is far from successful in curing the disease, and also in view of the fact that it is almost universally recognized at present that the thyroid gland seems as one link in a chain of organs involved, and its aberration of function forms but a small fraction of the series of abnormal events occurring in all the ductless glands. Thus we have a vicious circle of a most malignant sort, engendering a type of autointoxication but little understood today.

Let us, for the sake of argument, assume that the diseased thyroid gland is responsible for the picture clinically known as Graves' disease, still surgery does not seem to be the cure. Remove all of a diseased tonsil and your tonsillectomy is complete and satisfactory. There will be no further recurrence; the patient is better off for its absence. Leave a part of said tonsil and usually we are in course of time confronted with the need for another operation, the remaining portion having served as a root for the regeneration of the removed tissue. Remove the thyroid, however, and you ruin or kill your patient through the resulting myxedema. Leave a portion of the diseased thyroid in order to conserve the life of the patient, and as the lingering portion of diseased tonsil, not only will it continue poisoning the body with or without a period of apparent improvement or even cure, but sooner or later the entire gland is regenerated, and we have again a full-fledged case of exophthalmic goiter.

In view of the multiform theories and possibilities offered to explain the causes and *modus operandi* of exophthalmic goiter, it is evident that the syndrome is the most complicated state of affairs which it is the privilege of scientists to investigate. Hence we must deduce that the thyroid gland is not the only organ involved, but perhaps assumes but a small part of the entire responsibility of the clinical picture or the chain of events occurring in the pathologic physiology of the disease.

If such be the case, how can we expect a surgical intervention, through thyroidectomy or some other surgical operation attacking a local area, to overcome a disease caused by such widespread etiologic responsibility? Such an expecta-

tion is not only scientifically unreasonable, but has pr
to be clinically inconsistent.

As an evidence that surgeons are at sea regarding w
method of procedure to employ in exophthalmic goiter
tacit implication of their indecision regarding the treatm
of this disease) may be mentioned the fact that, during
past decade in different parts of the world and during
ments in the career of the same surgeon, surgical pr
dures differ, and for each method success almost unreser
is acclaimed. Here are a few of the most important pr
dures adopted:

(*a*) *Complete thyroidectomy.* Since this resulted in
chexia strumipriva in every instance, this method was
jected after some years as unnecessary and gave way to
following procedures:

(*b*) *Thyroidectomy of one lobe.* This usually prece
subsequent operations. It was found that here also
operation was not the one of "choice" because recurren
were too frequent, so that

(*c*) *Thyroidectomy of both lobes became the vogue.*
lowing this procedure, many things happened, among wh
were the accidental removal of the parathyroids with f
tetany, a temporary hyperthyroidism followed some t
later by a regeneration of lost thyroid tissue and recurre
of the Basedowian syndrome, and occasionally an acute
acerbation (postoperative) of hyperthyroidism, which
sulted fatally. Many surgeons considering the above p
cedures too radical resorted to

(*d*) *Ligation of one carotid artery* or

(*e*) *Ligation of both carotid arteries.* Ligation has
its purpose the partial interruption of the blood supply
the thyroid in order to diminish its functional activ
The collateral circulation in course of time becomes gr
enough to restore the former excess of vascularity, and
patient is as badly off as before. An occasional sim
taneous ligation of all four thyroid arteries has resulted
death. So that many surgeons resorted to

(*f*) *Ligation, unilateral or bilateral, followed some time later by thyroidectomy.* This subjects the patient to a plurality of operations and a high mortality rate, to say nothing of the therapeutic futility. A period occurred during which

(*g*) *Sympathectomy or resection of the sympathetic nerve was considered the means of cure, because it was followed by such prompt relief of the exophthalmos.* This was known as a Jaboulay or Jannesco operation, but soon fell into disuse because it failed to relieve the other symptoms of hyperthyroidism. Noting that many cases of exophthalmic goiter presented a large thymus, the operation of

(*h*) *Thymectomy, with or without thyroidectomy became the fad;* but because of the high mortality rate, this procedure has not become universally popular. Local interference with the excessive action of the thyroid gland was attempted by milder procedures, most important among which are

(*i*) *The injection of boiling water into the thyroid substance as advocated by Porter,* and

(*j*) *The injection of solutions of quinine and urea hydrochloride as advocated by Watson.* The author, although not prepared to accept the methods of Porter and Watson as based upon logical grounds, must say that since they are not fraught with the dangers of the aforementioned surgical procedures, they may, in severe cases of hyperthyroidism, be attempted as a supplementary measure where other therapeutic procedures do not yield results promptly enough.

Resection of the colon as a therapeutic measure in exophthalmic and simple goiter has a firm advocate in Sir Arbuthnot Lane. He reasons rightly when he states that the thyroid enlargement on the one hand and its hyperactivity on the other are merely evidences of an infection elsewhere acting as primary cause, and this infection, according to Lane, occurs in the colon, the removal of which overcomes the cause. He realizes the fallacy of attacking the thyroid itself, and his theory sounds plausible, but clinical evidences of cures are too few to warrant the adoption of this procedure in large measure.

With respect to thyroidectomy, the operation most popular with thyroid surgeons, the following may be said:

A happy medium, *i.e.*, the knowledge of how much or how little gland to leave *in situ* during thyroidectomy, has long been and still is a surgical controversy. For fear that the removal of too much thyroid will result in hyperthyroidism and the removal of too little in the need for subsequent "removal" of thyroid substance, surgeons have begun to employ figures with respect to how much of the gland is to be permitted to remain. Some state that one-sixth of the gland should be left behind, others one-fifth, still others one-third, and occasionally the opinion is advanced that "not more than one-eighth of the gland should be left behind lest there be a recurrence." All claim that some of it must be left behind, thus admitting that the thyroid gland is a vital organ (thanks to the experience of men who formerly removed the entire gland.) Do such controversies arise with respect to how much of the tonsils or of the appendix should be left behind?

It is not the purpose of the author unconditionally to condemn thyroid surgery. It is frankly admitted that a simple goiter, one which is not a hyperplastic, toxic thyroid, but a nontoxic, innocent enlargement of the thyroid gland marked enough to be discernible at a distance and one which has resisted local and general nonsurgical measures for a reasonable time, should be handed over to the surgeon for operation. Marked pressure symptoms where dysphagia and dyspnea are distressing, are also surgical conditions. In this category is included malignant changes: no matter what type of thyroid enlargement, any suspicion of malignant degeneration of the gland classifies the case as surgical. And here again we must include the secondary or "Basedowified" goiter, whether causing mechanical symptoms or not, as presenting surgical indications. In this latter type the thyrotoxicosis is secondary to the presence of that goiter, be it colloid, cystic, or otherwise, and as soon as the goiter is removed, the toxic symptoms disappear. These cases present the most gratifying surgical results. These conditions, however, are not the true, clear-cut cases of Graves' disease, a condition in which we unreservedly deny the right of surgery to interfere.

That Graves' disease or exophthalmic goiter is gradually becoming recognized as a disease strictly nonsurgical in nature, requiring nonoperative remedial measures, is now being conceded everywhere. This condition is no more a subject in the realm of surgery than is pneumonia or typhoid or scarlet fever. In pneumonia the surgeon's services may be required to correct a complicating empyema; in typhoid a peritonitis resulting from intestinal perforation; in scarlet fever a dangerous mastoiditis consequent upon a suppurative otitis media. Exophthalmic goiter, although not an acute infectious disease, is nevertheless one strictly outside the domain of surgery, unless dangerous pressure symptoms arise or malignant changes set in.

In view of the fact that many recurrences are seen in surgical clinics (not to mention the immediate mortality rate which is really higher than commonly stated) and also because of lack of ample proof of permanent cure from surgical procedures, farsighted surgeons in all parts of the world are now becoming skeptical with regard to their accustomed method of treatment of this disease and are beginning to lag in enthusiasm with respect to surgical interference in exophthalmic goiter. A rapid survey of the following opinions gleaned from various sources speaks for itself:

"As a general principle, in exophthalmic goiter surgery it is better to err in favor of conservatism, and when in doubt, it is by far safer to ligate than to thyroidectomize, and to resort to two ligations instead of three, one instead of two. It is better to have an imperfect result than it is to have death, inasmuch as the first alternative may be remedied by a subsequent operation, whereas the latter is beyond one's reach. * * *

"The *early mild forms* of hyperthyroidism in young individuals *should be treated medically.* We often see young women in schools and colleges, girls and debutantes react to overwork and undue excitement with a mild form of hyperthyroidism. They complain of nervousness, palpitation, insomnia, loss of appetite, muscular asthenia; the cardiac action runs up to 100 or higher; they have a moderate thyroid hyperplasia. This class of patients should be the triumph of medical treatment. Such patients should be treated with rest in bed for several weeks or months until the condition has subsided. Furthermore, their activities should be stopped and complete relaxation obtained. Here all physical as well as medicinal means which medical treatment possesses can be applied" (Crotti).

"How little is known today of the function of the thyroid even though surgeons have been removing them by the thousand! How many physicians still question the propriety of operating for toxic goiter and assume a skeptical attitude as to the reported results of surgical interference! It is my own belief that the present status of surgical therapy is but a stepping stone to the development of some method of arresting the toxic functional disturbances of the gland and that eventually other measures, perhaps nonoperative, will be forthcoming, that will deal with the cause rather than the effect of the deranged function and by removing the cause, break the vicious circle. * * * No matter how intelligently the surgical management of the case has been executed, satisfactory end results can not be obtained without quite as intelligent management of the after-treatment. If the latter is not carefully carried out, relapses will be more frequent, and the surgeon is dependent on the cooperation of the family physician. It has been our practice, on the patient's discharge, to send the physician a suggestive outline of the after-care. The patients must be protected as far as possible from unnecessary physical or nervous fatigue, and to this Ochsner adds the importance of rather rigid dietary regulation on which he lays great emphasis'' (Frazier).

''Reviewing the whole subject of the operative treatment of exophthalmic goiter, it seems to me that it may reasonably be doubted whether surgical treatment is not on the whole worse than useless. * * *

''None of the operations that have hitherto been practiced upon the gland, the thyroid vessels or the sympathetic are free from risk. Actual proof that any of them really cure the disease is at present wanting. The sympathetic operation, although it may, and probably does to a slight extent, diminish the exophthalmos, does not usually cure it completely, and may be followed by serious results, such as inflammation of the eye and even blindness. * * *

''The larger operations upon the gland itself, such as extirpation, are attended with so much danger as to make them undesirable. * * *

''With regard to ligature of the thyroid vessels, it still seems to me doubtful whether this proceeding is followed by cure sufficiently often to justify its performance'' (Berry).

According to Porter, there are three sources of dissatisfaction following thyroidectomy, viz.: First, failure to get relief from symptoms although there be no recurrence of goiter. Second, the immediate mortality is too high. Third, too many cases are seen which have gone beyond the point where the question of surgical relief can be entertained with reason.

According to McCarrison, hyperthyroidism is instigated by a toxemia due to intestinal stasis. This author suggests that surgical interference of the thyroid gland itself is usually not justifiable, but that the seat of the evil be attacked nonsurgically, *i.e.*, by the administration of laxatives and intestinal antiseptics. The fact that exophthalmic goiter and intestinal stasis are both most frequent among women may or may not be a mere coincidence, but we can not help admitting the suggestiveness of this combination with regard to etiologic relationship.

Even Crile, who is a strong advocate of surgery in exophthalmic goiter, says: "These hypersensitive patients may be killed by fear, even by worry; by slight injury or by surgical anesthesia; hence they require anociated treatment in the broadest sense, and in severe cases, the operation itself must be graded." This statement alone serves as sufficient warning against surgical intervention in these patients. The hypersensitive, explosive nervous system, continually dreading the knife, is made worse by the very prospect of surgery and often killed by the surgical shock and anesthesia. This termination occurs either while on the operating table or shortly afterwards.

"It is * * * impossible at present to give surgical treatment the preference over medical means" (Dieulafoy, quoted by Haeberlin).

"We are beginning to realize that all the ductless glands are intimately related and that in cases of ductless gland disarrangement we are dealing with a pluriglandular syndrome. We can expect ideal results when we can bring about a readjustment of these glands. At present we are not doing this, as would seem to be indicated by the frequency with which some syndromes persist even after most successful thyroidectomy" (Dean Lewis).

"The opinion of an eminent surgeon [this opinion, by the way is Kocher's endorsed by Chas. H. Mayo] that 90 per cent of all goiters can be so improved by medical treatment as to make operation unnecessary was probably based upon observation of the effect of rest, for rest is the common element in all the various forms of treatment that have proved successful" (Rice).

Statistics are a great source of error in surgery as elsewhere. The gloating over low mortality figures is a very misleading point to farsighted investigators. We must bear in mind the great truism mentioned by an eminent surgeon of bygone days, who decried the too thorough reliance upon statistics, exclaiming that "a dead patient is 100 per cent dead." Surgical statistics in the treatment of exophthalmic goiter *seem* to present information revealing (*a*) the operative mortality and (*b*) the percentage of cases relieved or cured. Regarding the first item, it may be said to the credit of surgery that the mortality, formerly as high as 20 per cent or 30 per cent, has now dwindled down, in the hands of competent surgeons, to as low as 5 per cent or 4 per cent, thanks to the refinement of technic by men devoted to thyroid surgery. Concerning the second factor, much may be said. Mere improvement is not sufficient reward to the patient for the risk that she has consented to undergo, nor is it sufficient compensation for the scar which she will present throughout life. Improvement is usually short-lived in almost every instance, the status merging back to the full-fledged condition with which the patient formerly suffered. Indeed, occasionally, the symptoms will return with greater vehemence than the occurrence of the original attack.

The word "recovery" as employed by surgical statisticians does not mean permanent *cure;* it means *surgical* recovery, *i.e.,* recovery from the effects of surgical shock and traumatism, or it means a degree of temporary relief from the Basedowian syndrome, or both. The surgical statistics do not go beyond the first few months or a year, and are incapable of presenting evidence leading to conclusive proof of *complete surgical cures of exophthalmic goiter.*

"The present low mortality of thyroid surgery in very competent hands has been obtained at the cost of many unfortunate victims as a rule" (Beebe). It is this improvement in mortality rate that makes the mind of the surgeon reason along surgical lines only, and although some of these men endeavor carefully to follow their patient through the course of months or even years after operation, the responses obtained from these patients through the mails and which constitute the basis of statistical figures regarding percentage of cases cured, improved, etc., are not reliable, since the patient himself or herself is incapable of proper clinical judgment. Beebe emphasizes the fact that the degree of severity of hyperthyroidism may seriously impair the efficiency of its victim without his being aware of it; "and while the patient may accurately report the state of his mind with respect to himself, he is not the most suitable person to decide with accuracy the state of his thyroid activity." The same observer has seen no statistics based upon a careful physical examination of the operated patient some months or years after the operation by physicians skilled in the disease and is convinced that such an examination would not tally with the present statistical figures of surgery. Beebe has never observed a complete operative cure in a case of exophthalmic goiter. This has also been the author's experience.

In the rare instances in which there is no recurrence of the symptoms within a year or two following thyroidectomy, the patient has obtained either (*a*) a natural cure, *i. e.*, the patient was one of those rare instances which tended toward spontaneous recovery, treatment or no treatment. A case of this sort gets well not because of, but in spite of, surgical treatment; or, (*b*) a nonsurgical cure. Careful surgeons will see that their patients be given prolonged nonsurgical treatment prior to operation, and many still more carefully outline nonsurgical treatment for a long time after operation is performed, as a result of which the asserted therapeutic value of the thyroid operation itself is reduced to a minimum, the credit of the possible relief or cure of necessity reverting to the nonsurgical procedures employed before and after the operation. Without the accompanying nonsurgical treatment, thyroidectomy is at once a complete failure not even yielding temporary relief in most instances. In realization of this fact, most careful surgical clinics see to it that a patient discharged after thyroid surgery is given a list of nonsurgical directions, without the religious observance of which, it is frankly admitted by the surgeons, the patient has little hope of the relief of symptoms. As an illustration, Crotti states: "When once a patient has been operated on, he becomes again a ***medical patient.*** He should be followed medically until cure is assured. The same medical principles which apply prior to the operation find their indication and usefulness after the operation: rest, change of environment, automobiling, sojourn in mountainous regions, are the best adjuvants of the surgical treatment." Further to exemplify, in Ochsner's clinic the following list of printed directions is given to each discharged patient:

1. You should avoid all excitement or irritation, such as attending receptions, shopping, church work, or politics.
2. You should get an abundance of rest by going to bed early and taking a nap after luncheon.
3. You should have an abundance of fresh air at night, consequently you should sleep with wide open windows or on a sleeping porch.
4. You should eat and drink nothing that irritates the nervous system like tea, coffee, or alcohol. Of course, you should not use tobacco in any way.
5. You should eat very little meat. If you are very fond of meat, take a little beef, mutton, or breast of chicken, or fresh fish once or twice a week, or at most three times a week.
6. You should drink a great deal of milk or eat things that are prepared with milk, such as milk soup, milk toast, etc.; cream and buttermilk are especially good for you.
7. You should avoid beef soup or beef tea or any kind of meat broths.
8. You should eat an abundance of cooked fruits and cooked vegetables or very ripe raw fruits, or drink fruit juices prepared out of ripe fruits.
9. You may eat eggs, bread, butter, toast, rice, cereals.
10. You should drink an abundance of good drinking water, or if this is not available, you should boil your drinking water for twenty minutes or drink distilled water."

Ochsner states that with the exception of a very number of cases in which an insufficient amount of the has been previously removed or in which the remnar at the primary operation had increased in size, in p cally all the cases which had recurred, it was found a invariably that the patients had disregarded the abo rections concerning diet, rest and hygiene, following operative treatment, or they had been permitted to r to their homes without definite instructions in this dire Is not this an outspoken confession of the failure of su in exophthalmic goiter? Note that the real basis of is frankly stated to be the above mentioned nonsu procedure without which surgery is admittedly a fa These rules alone, properly carried out (and this can r refuted by thyroid surgeons), are capable of curing r all cases of exophthalmic goiter without surgical inte tion, all things being equal.

In addition to the futility of surgical interference i ophthalmic goiter, let us enumerate a few of the very other objections which the internist might advance in regard:

1. The surgical mortality rate is higher than the s 5 per cent, while the nonsurgical mortality, if treatme not too greatly postponed, is practically nil.

2. Many patients succumb to immediate postoper acute exacerbations of hyperthyroidism.

3. Recurrences of goiter and symptoms mean mu operations with the attending dangers.

4. The subject of exophthalmic goiter, hypersensiti the extreme degree may die of fear or of worry ove operation, or even by light infection following surgical cedures. Indeed, experienced surgeons, cognizant of facts, often prefer to do an enucleation or thyroidec in several stages.

5. The frequent presence of sugar in the urine is a traindication to surgical procedure.

6. A great danger in these cases is death by status lymphaticus.

7. The occasional removal of the parathyroids during thyroidectomy with resulting tetany, is by no means a rare occurrence.

8. Injury to the recurrent laryngeal nerve directly through the operation or subsequently by pressure of scar tissue, is not uncommon, leading to paralysis of the vocal cords.

9. The frequently occurring postoperative myxedema as a result of thyroid enucleation is worse than Graves' disease. Kocher states that the average life of a case of myxedema is seven years.

10. In many instances, surgery has so devitalized the patient that the prognosis is rendered doubtful even when under the care of a competent internist. The surgical shock, the postponement of the proper nonsurgical measures during all this time, and frequently the mental attitude of the patient who is so thoroughly disgusted with everything and everybody, including the medical profession, that all initiative to get well is lost,—all these factors diminish the prospects for complete recovery.

The real difficulty in the treatment of hyperthyroidism has been that both surgeons and internists have looked for immediate results and drawn their deductions and statistics accordingly. The eagerness to generalize hastily instances of apparent relief or apparent failure on the part of the therapeutists—surgical and nonsurgical—has been the stumbling-block in the way of therapeutic progress in the treatment of this disease. Surgeons have frequently succeeded in giving immediate temporary improvement, but more frequently these patients suffer a relapse which is sometimes of greater intensity than the primary shock of hyperthyroidism. Internists, even when proper measures are instituted, are impatient when results are not immediate, and turn their cases over to the surgeon. So that here also we are tending toward a vicious circle in the thera-

peutics of the disease. The truth of the matter is tha
surgeon should show less haste, and the internist mor
tience, in the treatment of these cases. I base this co
sion upon the lack of statistics proving permanent c
in exophthalmic goiter on the part of the surgeons,
upon the presence of a large number of permanent c
effected by some internists who skillfully and patientl
ploy the proper nonsurgical procedures through the le
of time necessary to bring about complete recovery.
object is to suggest to the profession to avoid haste i
sorting to surgery and to be more patient in the use of
surgical measures, and when a general practitioner
that his case has been treated nonsurgically for a reaso
length of time without satisfactory improvement, it is
ther suggested that, instead of turning the patient ov
the surgeon for operation, an internist who has had e
tional experience in thyroid therapy, be consulted.

Now what has the internist experienced in thyroid
apy to offer in the treatment of Graves' disease? Th
swer can be summarized by saying that first, his discha
patients present no mutilating scars; secondly, his c
are free from such complications as myxedema, tetany,
the others mentioned under surgical considerations; thi
he has no mortality rate in cases brought to him that ar
already in the moribund state; and fourthly, his pati
treated by an endeavor to overcome the exciting cause
discharged permanently cured, relapses occurring ra
if ever.

To emphasize, the following opinions are offered:

"The surgeon is apt to do too much and the physicia
little" (Musser).

"In Volume LXV (1911) of Guy's Hospital Reports,
Hale White records the results of an attempt upon his
to trace the history of patients discharged after me
management during the last twenty years, and he finds
in about 80 per cent the recovery has been permanent.
my own personal and consultation practice I have had

opportunity to observe a number of patients for periods varying from a few months to twenty-five years after apparent recovery under nonsurgical treatment. In but one instance has there been relapse, and in no case had death occurred from any condition with which Graves' disorder could be causatively associated'' (Solomon Solis-Cohen).

In a personal communication, Professor Solomon Solis-Cohen, whose wide experience as internist stamps him as an authority on this subject, expresses the following clear-cut views, pregnant with significance:

1. Graves' syndrome is *one* of a number of related syndromes shading into one another (like a spectrum of which it may be considered the red, while Raynaud's syndrome is the violet) showing varying degrees of unbalance or inco-ordination (*ataxia*) in the vegetative (autonomic) nervvous system and its endocrine appendages. This basic condition of *autonomic ataxia* is generally congenital and commonly inherited, but in rare instances appears to have been acquired. Under the incidence of various exciting causes and local determinants, varying syndromes appear in the same individual at different periods of life—in different members of the same family—in different families of the same clan.

2. The thyroid enlargement, with or without hyperactivity and later hypoactivity, is secondary; and its results are therefore *epiphenomenal* and not *fundamental.* It is an important incident, but only an incident.

3. The thyroid tumor may or may not call for operation, as a tumor; it may or may not call for operation as a source of toxic disturbance; it may or may not call for operation as a means of breaking a vicious circle; but operation is never curative of the basic condition, which still remains to be treated.

4. Treatment of the basic condition may render operation needless from any viewpoint. It does not remove the congenital tendency, but controls this, so that overt morbid results are prevented.

5. The thyroid tumor and its direct results may be tre successfully without operation. There are many meas none infallible, none of universal application. Individ zation is needed.

6. Operation should not be done until a sufficiently longed trial of rest and other appropriate measures been had, without good result.

7. Exceptions to this rule are: (*a*) when the case is too late, and urgent mechanical or toxic symptoms are ent; but here again the toxic symptoms must not be character that contraindicates operation; (*b*) when th tient's social condition is such that he or she can not as required. In either event the operation should b slight as possible, and there should be good, persistent a care.

McCarrison, whose experiences with diseases of the roid gland are unsurpassed, makes the following state in his excellent treatise, "The Thyroid in Health and ease:"

"In four out of eleven 'cures' affected by operation a Thomas' Hospital, there was no evidence of Graves' ease found on microscopical examination (Mackenzie that in 36 per cent of these cases which were classe 'cures' we must admit either an error in diagnosis or clude that the thyroid gland does not share the usual dences of Graves' disease in a very much higher propo of cases than has hitherto been supposed.

"The practice of operative interference with the thy gland in all cases of Graves' disease at sight and wit applying all the resources of our art in the detection o cause, as is now a very common custom, is one which not be too strongly deprecated. I am convinced that the number of cases in which thyroidectomy is perfor will become smaller and smaller and its practice, excep cases which have baffled the most painstaking invest tion, will ultimately be abandoned."

It would be superfluous to publish the numerous other opinions of like nature, all of which, coupled with the aforementioned statements of surgeons indicating hesitancy, reveal this conclusion: The profession is about ready to change its views with regard to the therapy of exophthalmic goiter, and this change is decidedly in favor of a rejection of surgery.

Careful nonsurgical management, then, is capable of completely and permanently curing nearly every case of hyperthyroidism. The occasional exception not responding to nonsurgical measures is not an instance of genuine Graves' disease, but is one of malignant degeneration of the thyroid gland, a case of toxic symptoms superimposed upon a long-standing nontoxic goiter, or a case brought to the clinician's attention in a moribund condition. The author, in unison with others interested in thyroid therapy, does not hesitate to conclude that he has been able to cure every case of Graves' disease that was able to come to his office; this was accomplished in from six months to two years, depending upon the exigencies of the case treated. Strict individualization of the case in hand is the dominating principle of treatment. The proper medical attendant, the proper social atmosphere, and the right kind of dietetic, hygienic, medicinal, psychotherapeutic, electrotherapeutic and other measures properly applied for the required length of time should, in the presence of a fair degree of cooperation, yield 100 per cent of cures.

The author can not emphasize too strongly the following important fact deduced from theoretical and practical observations of the physiology, pathology, and symptomatology of thyroid affections: The primary etiology of exophthalmic goiter is never to be found in the thyroid gland itself; in other words, this disease is secondary, depending upon a cause or causes outside the thyroid gland. It is for this reason that surgery, unable to remove the cause of Graves' disease, is a fallacious procedure, and that nonsurgical measures, endeavoring to restore the balance tween the physiologic functions and relations of the turbed organs of the body, overcoming the various vici circles, bring about a permanent restoration of health

APPENDIX

The following are some of the author's articles on the subject of exophthalmic goiter, which form the basis of several of the chapters of this volume:

Nonsurgical Treatment of Exophthalmic Goitre, Merck's Archives, January, 1913.

Nonsurgical Treatment of Exophthalmic Goitre, New York Med. Jour., Nov. 27, 1915.

Nonsurgical Cures of Exophthalmic Goitre, New York Med. Jour., April 28, 1917.

Exophthalmic Goitre, Remarks on the Symptomatology, Prognosis and the Nonsurgical Treatment, Archives of Diagnosis, (New York) October, 1917.

The Body and Mind in the Nonsurgical Treatment of Exophthalmic Goitre, New York Med. Jour., Nov. 30, 1918.

The Circulatory System in Exophthalmic Goitre, International Clinics, Vol. I, series 29.

Course and Prognosis of Exophthalmic Goitre, Archives of Diagnosis, (New York) Jan., 1919.

The Surgeon and Internist in the Nonsurgical Treatment of Exophthalmic Goitre, New York Med. Jour., Jan. 4, 1919.

Successful Therapy of Exophthalmic Goitre, New York Med. Jour., Feb. 22, 1919.

Peculiarities in the Symptomatology of Exophthalmic Goitre, Med. Record, (New York) March 1, 1919.

The Etiology of Exophthalmic Goitre, Charlotte Med. Jour., March, 1919.

The Prevention of Goitre, American Medicine, (New York) April, 1919.

The Nonoperative Treatment of Toxic Goitre, In tional Clinics, Vol. II, series 29.

Shell Shock (?) in Soldiers, New York Med. Jour., J 1919.

Rational Therapeusis of Exophthalmic Goiter, End ology, Oct.-Dec., 1919, iii, 467-484.

BIBLIOGRAPHY

Abrahams, R.: Philadelphia Med. Jour., Feb. 9, 1901.

—. Med. Rec., New York, June 20, 1914.

Abrams, Albert: Diagnostic Therapeutics, Rebman Co., New York.

Aikens, W. H. B.: New York Med. Jour., July 8, 1916.

Alexander: Med. Klin., 1917, xiii (Abst. Endocrinology, ii, No. 3).

Anders, James M.: New York Med. Jour., Oct. 21, 1916.

—. Practice of Medicine, ed. 12.

Aran: Bull. Acad. Méd., November, 1860, xxvi.

Arsimoles and Legrand: Ann. Medico-Psychol. (Paris) 1914, p. 154.

Azam, J.: Thèse de Paris, 1907.

Baar, G.: Endocrinology, vol. i, 1917.

Bailey, Pearce: Jour. Am. Med. Assn., Dec. 28, 1918.

Balfour, D. C.: Med. Rec., New York, Nov. 16, 1918.

Ballet and Delherm: La Bulletin Médicale, Oct. 19, 1907.

Ballet and Enriquez: Congrès. des Méd. Alien. et Neur. de Fr. et des Pays de lang. franç., 6e session. Bordeau, 1895, T. II. (Roussy)

Barker, G.: The Simpler Natural Bases, London, 1914.

Barker, Lewellyn, F.: Jour. of Am. Med. Assn., Oct. 5, 1907.

—. Nervous and Mental Symptoms in Exophthalmic Goitre, Jour. of Am. Med. Assn., Aug. 3, 1918.

Barr, J.: Abstract Endocrinology, ii, No. 4.

Baruch: Zentralbl. of Chir. No. 10, 1912.

Bassinger, H. R.: Jour. Infect. Dis. (Chicago) 1917, xx, 131.

Bate, R. Alexander: Medical Bulletin, September, 1914.

Béclère: Bull. de la Soc. Méd. d. Hôp., Oct. 12, 1894.

Beebe, S. P.: Med. Rec., New York, April 14, 1917.

—. Jour. of Am. Med. Assn., Oct. 15, 1917.

—. Med. Rec., New York, Feb. 9, 1919.

Beebe and Beveridge: New York Med. Jour., Dec. 25, 1915.

Bensley, R. R.: Am. Jour. Anat. (Philadelphia) 1916, xix, 37.

Benard, Claude: Thèse, Paris, 1882.

Bérard, Leon: Bull. de l'Acad. de Méd., Paris, Nov. 28, 1916.

Berkley, Henry J.: Johns Hopkins Hospital Bulletin, September, 1908.

Bernhard: Correspondenz-Blatt für Schweizer Aerzte, Jan. 19, 1918.

Bernhardt, M.: Berl. klin. Wchnschr., July 2, 1906.

Berry, James: Diseases of the Thyroid Gland.

Billings, Frank: Jour. Am. Med. Assn., (Abstract) Jan. 8, 1916.

Bircher: Zentralblatt f. Chir., 1912, xxxix, 15.

Bishop, H. D.: Cleveland Med. and Surg. Reporter, November, 1905.

Blair, V. P.: Jour. Am. Med. Assn., June 5, 1915.
Boggs, Russell: Interstate Med. Jour., April, 1917.
Boir, C: Klin. Monatsb., f. Augenheilk., Berlin, 1917, No. 728, p. 59.
Brissaud: Mercredi Médicale, No. 34, 1895.
Brooks, Harlow: Tr. New York Acad. Med., Feb. 7, 1918.
—. Am. Jour. Med. Sc., November, 1918.
Brown, O. H.: Asthma, C. V. Mosby Co., St. Louis.
Bumsted, C. V. R.: Med. Rec., New York, March 20, 1915.
Burget, G. E.: Am. Jour., 1917, 44, 492.
Butler, G. R.: Diagnostics of Internal Medicine, ed. 2, pp. 546, 547, 548.

Cannon, W. B.: Bull. Johns Hopkins Hosp. (Baltimore) 1916, xxvii, 247.
—. Boston Med. and Surg. Jour., 1916, clxxv.
Cannon and Cattell: Am. Jour. Physiol., 1917, xli, 74.
Caro: Berl. klin. Wchnschr., 1907, xliv.
—. Deutsch. Med. Wchnschr., 1915, xli, 1009.
Carpi: Berl. klin. Wchnschr., 1910, xlvii.
Ceballos, A. and Bacigalupo, G.: Revista de la Asociacion Medica, Ar
tina, Sept., xxvii, No. 154, pp. 225-406.
Claisse, Paul: La Clinique, Jan. 5, 1906.
Cobb, Ivo Geikie: The Organs of Internal Secretion, 1919.
Coenen: Berl. klin. Wchnschr., 1911, xlviii.
Cohen, Solomon Solis: Am. Jour. Med. Sc., July, 1912.
—. International Clinics, Vol. 3, series 19.
—. Abstract of Discussion, Jour. Am. Med. Assn., Aug. 25, 1917.
Coleman, G. B.: Surg. Gynec. and Obst., January, 1915.
Coleman, Warren; Musser and Kelley: Practical Treatment.
Coliceti, P.: Policlinico, Rome, Dec. 25, 1918.
Crile, George W.: Jour. Am. Med. Assn., Aug. 25, 1917.
Crookshank, F. G.: Monthly Cyclopedia and Med. Bulletin, August, 1914.
Crotti, André: Jour. Am. Med. Assn., Jan. 11, 1913.
—. Jour. Am. Med. Assn., Feb. 22, 1913.
—. The Thyroid and Thymus, Lea and Febiger, Philadelphia.
Cunningham, D. J.: Text Book of Anatomy, 1902.
Curschmann, H.: Ztsch. f. klin. Med., 1912, lxxvi.
Cyriax, R. J.: Lancet, London, 1916, i.

Dalrymple: Jour. Morb. Anat., 1828, p. 43.
DeSchweinitz, G. E.: Diseases of the Eye, ed. 7, W. B. Saunders Co.
Dock, George: Musser and Kelley's Practical Treatment, vol. i.
Dowd, Chas. N.: Jour. Am. Med. Assn., Aug. 25, 1917.
Drysdale, H. H.: Ohio State Med. Jour., 1916, xii.
Dubois, E. F.: Arch. Int. Med., Chicago, 1916, xvii.

Eastman, T. B.: Jour. Indiana Med. Assn., 1916, ix.
Ebstein: Quinzaine Thérapeutique, Nov. 10, 1913.

Eddy, N. B.: Canadian Med. Assn. Jour., Toronto, March, 1919.
Editorial "Music and Health," New York Med. Jour., Aug. 7, 1915.
Ellis, A. G.: Med. Rec., New York, (Abstract) March 16, 1918.
Ellis, Havelock: Man and Woman, ed. 4.
Elsner, Henry: Am. Jour. Med. Sc., May, 1914.
Endocrinology: Editorial, The Interrelationship of the Thyroid and the Adrenals, 1917, vol. i, No. 4.
Endocrinology: Editorial, ii, No. 4, 1918.
Eppinger and Hess: Vagotonia, translated by Kraus and Jelliffe, 1915.
Epstein, W.: Therap. Monatsh., December, 1910.
Etienne, G. and Richard, G.: Bull. de la Soc. d. Hôp. de Paris, Dec. 20, 1918, p. 42, No. 36. (Abst. Am. Med. Assn., Mar. 29, 1919.)

Faber: Deutsch. Med. Wchnschr., 1907, No. 42.
Fellenburg, R. von: Cor. Bl. f. Schw. Aerzte, Basel, 1915, xlv.
Frazier, Chas. H.: Pennsylvania Med. Jour., January, 1916.
—. Pennsylvania Med. Jour., May, 1918.
Freud, Herman: Deutsch. Ztschr. f. Chir., xxxi.
Freund: München Med. Wchnschr., 1, iv, No. 17.

Gauthier, Char. de: Memoirs presenté à l'Academie de Médecine, September, 1885.
Gebele: Beitr. z. klin. Chir., 1910, lxx, 1.
Geigel: Würtzburger Med. Ztschr., 1866, vii.
Gierke: München med. Wchnschr., April 16, 1907.
Goetsch, E.: Jour. Am. Med. Assn., 1916, xlvii.
Gordon and Jagic: Wien. klin. Wchnschr., 1908.
Gordon, M. B.: Endocrinology, ii, No. 4.
Graefe: Arch. f. Ophth., 1857, iii, 278.
Greenfield, Wm. E.: Brit. Med. Jour., Dec. 9, 1893.
Gries, G. W.:Am. Jour. of Roentgenology, June, 1917.
Gudernatsch, J. F.: Arch. f. Entwickmech. d. Organismen, 1912, p. 35.
Guthrie, Donald: Jour. Am. Med. Assn., Aug. 31, 1918.

Haeberlin, John B.: New York Med. Jour., May 5, 1915.
—. New York Med. Jour., May 29, 1915.
Hallion; Bull. Soc. Biol., July 6, 1907.
Hallion and Alquier: Bull. Soc. Biol., 1908, 64.
Hammill, R. C.: Med. Clin. of Chicago, 1916, 2, p. 85.
Hansemann, von: Berl. klin. Wchnschr. Oct. 30, 1915.
Harrower, Henry R.: Lancet-Clinic, Cincinnati, 1916, p. 116.
—. Med. Rec., New York, Aug. 3, 1918.
Hartshorne: A System of Medicine, Reynolds, 1880, iii.
Hartshorne, I.: Med. Rec., New York, (Abstract) Feb. 27, 1915.
Hasebroeck: Die Erschütterung in der Zanderschen Heilgymnastik in physiologischer und therapeutische Beziehung, Hamburg, 1890.

Hernaman-Johnson, P. and White, P. C.: Lancet, London, 1916, cx (Abst. Endocrinology, vol. i, 1917).
Hernaman-Johnson, P.: Lancet, London, 1916, ii, 920.
Herring: Quart. Jour. Exper. Phys., 1916, lx, 391.
Hertoghe, E.: Med. Rec., New York, Sept. 19, 1914.
Hertzler: Jour. Am. Med. Assn., 1911, lvii, 2076.
Hirschl: Wien. klin. Wchnschr., xix, No. 62.
Hirst, B. C.: International Clinics, ii, series 27.
Hofbauer, L.: Med. Blätter, 1907, xxx.
Hoppe, Herman H.: Jour. of Nervous and Mental Diseases, April, 1918.
Hoskins, E. G.: Jour. Am. Med. Assn., 1910, lv, 1724.
Hoskins, E. R.: Endocrinology, ii, No. 3.
Huhle: Deutsch. Arch. f. klin. Med., 1914, cxiii.
Hunt, Reid: Jour. Biol. Chem., New York, 1905-6, 1, 33-34.
Hunziker, H.: Correspondenz-Blatt für Schweizer Aerzte, Basel, Feb. 9, No. 6, p. 48.
Hutinel, V.: Arch. de Méd. d' enf., Paris, December, 1918, xxi, No. 12.

Imboden, Harry M.: Med. Rec., New York, (Abstract) Feb. 27, 1915.

Jaboulay: Bull. de l'Acad. de Méd., 1897, xxxvii.
Jackson and Mead: Boston Med. and Surg. Jour., 1908, clviii, No. 7.
James, Wm.: Principles of Psychology, Henry Holt & Co., New York.
—. The Will to Believe, Longmans, Greene & Co., New York.
Janney, Nelson W.: Med. Rec., New York, (Abst.) Feb. 24, 1917.
—. Arch. Int. Med., August, 1918.
Janney and Isaacson: Proc. Soc. Exp. Biol. and Med., 1917, xiv, 99.
—. Jour. Am. Med. Assn.: (Editorial, Jan. 8, 1916.)
—. Jour. Am. Med. Assn.: (Editorial, Sept. 8, 1917.)
—. Jour. Am. Med. Assn.: (Abstract, Jan. 26, 1918.)
—. Jour. Am. Med. Assn.: (Editorial, Mar. 23, 1918.)
—. Jour. Am. Med. Assn.: (Editorial, Dec. 14, 1918.)
—. Jour. Am. Med. Assn.: (Editorial, Dec. 28, 1918.)

Kaplan, D. M.: Endocrinology, i, No. 2, 1917.
Kappenburg, B. D. G.: Med. Tydschr. v. Geneisk., Amsterdam, 1916, ii.
Kappis: Mitt. A. D. Grenzgeb. D. Med. U. Chur., 1910, xxi, No. 5.
Kendall, E. C.: Jour. Am. Med. Assn., June 19, 1915.
—. Jour. Am. Med. Assn., lxvi, 1916.
—. Jour.-Lancet, 1917, pp. 37, 768.
—. Endocrinology, vol. ii, No. 2, 1918.
—. Jour. Am. Med. Assn., (Abst. of Discussion) Sept. 14, 1918.
Kjlstad, S.: Norsk. Magazin for Laegevidenskaben, Christiania, March, 1 No. 3, p. 79.
Klinger, P.: Correspondenz-Blatt für Schweizer Aerzte, Basel, April 27, 1
Klose, Lampé and Lisegang: Beit. z. klin. Chir., 1912, lxxvii.

Kocher: Arch. f. klin. Chir., 1908.

—. Arch. f. klin. Chir., Berlin, October, 1908, No. 4.

Koeben: Dissert. inaug., Berlin, 1855.

Kohane: Wien. klin. Wchnschr., 1915, xxviii, 148.

Kojima, M.: Quart. Jour. Exper. Physiol., London, 1917, xi, 255-351.

Kummer, E.: Endocrinology, i, 1917.

Kuriyama, S.: Am. Jour. Physiol., July, 1917.

Lampé: Deutsch. med. Wchnschr., 1912, xxxviii.

Landström: Uber Morbus Basedowii, 1907.

Lane, Arbuthnot: Jour. Am. Med. Assn., (Abstract of Discussion) Aug. 31, 1918.

Lanz, O.: Nederlandsch. Tydschrift voor Geneeskunde, Amsterdam, Feb. 24, 1916.

Ledoux-Lebard: Rapport au 4• Congrès de Physiotherapie de médecine de langue française, April, 1912.

Lemel, N. J.: Nederlandsch Tydschrift voor Geneerskunde, Amsterdam, No. 4, (Abstract, Jour. Am. Med. Assn., Jan. 9, 1915).

Leniez: Progrès Méd., Nov. 21, 1916.

Lévi, Léopold: Presse méd., June 10, 1918.

Lévi, Léopold and Rothschild, H. de: La Petite Insuffisance Thyroïdienne et son Traitement.

Levy: Am. Jour. Physiol., 1916, xli, 492.

Lewis, Dean: Jour. Am. Med. Assn., (Abstract of Discussion) Oct. 3, 1914.

Lian: Presse Méd., December, 1918.

Lichty, John A.: Pennsylvania Med. Jour. (Abstract) June, 1914.

—. Pennsylvania Med. Jour. January, 1919.

Lorand, C. R.: De la Soc. Biol., xvi, 19 mars, 1904.

Lucien, M. and Parisot, J.: Revue Médical de l'Est, May 15, 1909.

Ludin: Centralbl f. d. Grenzgeb. d. Med. u. Chir., Jena, xviii, No. 3.

McCarrison: The Thyroid Gland, 1917.

McCord, C. P. and Marinus, C. J.: Endocrinology, vol. ii, No. 3.

MacCallum, W. G.: Medical News, Oct. 30, 1903.

—. Medical News, April 8, 1905.

—. Jour. Am. Med. Assn., Oct. 5, 1907.

Mackenty: New York Med. Jour. (Abstract) Feb. 23, 1918.

Mackenzie, H. W. G.: Lancet, London, September, 1890.

Mackenzie, Hector: Brit. Med. Jour., Oct. 28, 1905.

—. Lancet, London, 1916, cxci, 815.

Mackinnon, R.: Brit. Med. Jour., 1916, iii, 48.

Manley and Marine: Jour. Am. Med. Assn., 1916, lxvii, 260.

Mannaberg: Wien. klin. Wchnschr., 1913, No. 18.

Marine, D.: Surg. Gynec. and Obst., 1917, xxv, 272.

Marine and Kimball: Jour. Lab. and Clin. Med., 1917, iii, 40.

Marine and Lenhart: Jour. Exper. Med., 1910, xii, 311.

Markoe, J. W.: Jour. Am. Med. Assn. (Abstract of Discussion,) S
1918.
Maurice: Lyon Médical, Oct. 20, 1912.
Mayo: Surg. Gynec. and Obst., March, 1914.
Mayo, C. H.: Jour. Am. Med. Assn., Oct. 3, 1914.
—. Jour. Am. Med. Assn., Aug. 31, 1918.
—. Jour. Am. Med. Assn., (Abstract of Discussion) Sept. 14, 1918.
Mayo and Plummer: Med. Rec. (Abstract) Oct. 16, 1915.
Mays, Thos. J.: New York Med. Jour., May 5, 1917.
Means, J. H. and Aub, J. C.: Jour. Am. Med. Assn., July 7, 1917.
Melchior, E.: Berl. klin. Wchnschr., 1917, liv, 35.
Merck's Archives: (Abstract,) July, 1914.
Miller: Lancet-Clinic, Cincinnati, May 25, 1907.
Miller, Chas. S.: New York Med. Jour., Dec. 29, 1917.
Mills, C. A.: Am. Jour. of Physiol., July, 1918.
Möbius, O.: Schmits Jahrb., 1886, ccx.
Moon, R. O.: Brit. Med. Jour., Nov. 30, 1918.
Morris, Henry: Human Anatomy, ed. 3, 1905.
Müller: Med. klin., 1910, No. 34.
Münsterberg, Hugo: Psychotherapy, Moffat, Yard & Co., New York.
Musser: Am. Jour. Med. Sc., cxliii.

Ney, K. W.: New Orleans Med. and Surg. Jour., 1917, lxix, 546, (En
Vol. i, 1917).
Niles, Walter L.: Med. Rec., New York, Feb. 27, 1915.
Nordentoft, S.: Ugeskrift for Laeger, Copenhagen, 1918, p. 80.

Ochsner: Ann. Surg., 1916, lxiv, 385.
O'Day, J. C.: Internat. Jour. Surg., 1916, xxix, 312.
Olivier: Paris Medical, Oct. 5, 1918.
Oswald, A.: Centralbl. f. Physiol. Leipz. u. Wien., 1915, p. 30.
Ott and Scott: Jour. Pharm. and Exper. Ther., 1911-12, iii, 625.

Pal: Semaine Méd., Jan. 28, 1914.
Parisot, J.: Le Journal Méd. Français, March 15, 1913.
Pettavel: Deutsch. Ztschr. f. Chir., 1912, cxvi.
Pfahler and Thrush: Therap. Gaz., 1906, iii, p. 15.
Pfahler, Geo. E. and Zulick, J. D.: Am. Jour. of Roentgenology, Feb
1916.
Pfeiffer: München med. Wchnschr., 1907, No. 24.
Phipps, C.: Boston Med. and Surg. Jour., 1916, clxxiv, 73.
Piersol, Geo. A.: Human Anatomy, 1907.
Pietrowicz, Stephen R.: Jour. Am. Med. Assn., Jan. 8, 1916.
Pisani, O.: Revista Ibero-Am. de cien. Med., Madrid, June, 1917.
Plummer, H. S.: Jour. Am. Med. Assn., Aug. 30, 1913.
—. Am. Jour. Med. Sc., Dec., 1913.

Plummer, H. S.: Med. Rec., New York, (Abstract) Oct. 16, 1915.
Porter, Miles F.: New York Med. Jour., Feb. 15, 1919.
Pottenger, F. M.: Jour. Am. Med. Assn., Aug. 3, 1918.
Prebel, Robt. B.: Jour. Am. Med. Assn., Oct. 5, 1907.

Rautman: Mitt. a. d. Grenzgeb. d. med. u. Chir., Jena, xxviii, No. 3.
Reede, E. H.: Washington Med. Ann., 1916, xv, 230-36.
—. Med. Rec., New York, Mar. 17, 1917.
Reisman, D.: Jour. Am. Med. Assn., 1916, lxvi, 1381.
Rénon and Delille: Bull. Soc. méd. d. Hôp., June 19, 1918.
Ricaldoni, A.: Anales Facultad de Med. Montevidio, 1917, ii, 669.
Rice, James F.: Med. Rec., New York, July 20, 1918.
Richter, G.: Med. Herald, (Kansas City) 1916, xxxv, 307.
Robertson, T. B.: California State Jour. Med., San Francisco, 1917, xv, 491.
Rogers, J.: Jour. Am. Med. Assn., Sept. 2, 1911.
—. Jour. Am. Med. Assn., (Abst. of Discussion,) Aug. 25, 1917.
Rössle: München med. Wchnschr., 1907.
Roth: Deutsch med. Wchnschr., 1910, xxxvi.
Roussel, A. E.: Pennsylvania Med. Jour., January, 1919.
Roussy, Gustave: Les Lesions du Corps Thyroide dans la Maladie de Basedow, Paris, Masson et Cie, 1914.

Sahli, Hermann: A Treatise on Diagnostic Methods, ed. 2, 1918.
Sainton, P. and Fayolle, P.: Bull. Méd., Paris, July, 1, 1914.
Sainton and Gastaud: Bull. Méd., Paris, July 23, 1913.
Sajous, C. E. de M.: Merck's Arch., May, 1914.
—. New York Med. Jour., Aug. 1, 1917.
—. New York Med. Jour., Sept. 1, 1918.
—. Pennsylvania Med. Jour., Jan., 1919.
—. Address before American Therapeutic Society, June 6th, 1919.
Salzman, S.: Am. Jour. Obst., New York, 1916, lxxiv, 812.
Santa Maria, R. S. de: Tuberculosis Hyperthyroidism, Siglo med., Madrid, May 4, 1918.
Schafer: Archiv. f. mikro. Anat. u. Entwick., xlvi, 895.
Schoenborn, S.: Arch. f. exper. Path. u. Pharmakol., lx, 1909.
Schwarz: Wien. klin. Wchnschr., 1908, No. 35.
Secher, K.: Ugesk. f. Læger, Copenhagen, Oct. 10, 1918.
Seymour, M.: Boston Med. and Surg. Jour., 1916, clxxv, 568.
Sheehan, Joseph E.: Med. Rec., New York, Oct. 6, 1917.
Shurley, B. R.: Jour. Am. Med. Assn., 1916, lxvii.
Sielmann: München med. Wchnschr., 1914, lxi, 2125.
Simonton, Thomas G.: Pennsylvania Med. Jour., February, 1918.
Simpson: Med. Rec., New York, Sept. 4, 1915.
Smith, Fred M.: Jour. Am. Med. Assn., Feb. 15, 1919.
Smith, G. E.: Jour. Biol. Chem., 1917, xxix, 215.
Smith, J. H.: Jour. Mental and Nervous Dis., New York, 1916, xlv.

Smith and Broders: Jour. Am. Med. Assn., Jan. 10, 1914.
Smorzarsky: Russky Vrach, Petrograd, June 27, xiii, No. 24.
Snow, Wm. Benham: Archives of the Roentgen Ray and Allied Phe
September, 1908.
Stanton, E. MacD.: Am. Jour. Med. Sc., Philadelphia, 1918, clvi, 36
Stegman: München med. Wchnschr., 1905.
Stellwag: Wien. Med. Jahrb. 1869, p. 25.
Stengel: Pennsylvania Med. Jour., 1906.
Stern, S.: Med. Rec., New York, (Abstract of Discussion) Sept. 28
Stiles, Percy G.: Nutritional Physiology, ed. 3.
Stoney: Archives Roentg. Ray, January, 1913, p. 320.
Stoney, F. A.: Lancet, London, 1916, ii, 777, (Abst. Endocrin. i, 1917
Swan, John M.: Internat. Clin., 26th series, ii, iii.

Taylor, J. Madison: The Monthly Cycl. Pract. Med., April, 1906.
Taylor, Wm. J.: Cleveland Med. Jour., 1906.
Thaon: Thèse, Paris, 1905.
Thompson, Gilman: Am. Jour. Med. Sc., 1916, cxxxii, 835.
Thomas, Wm. M.: Surg. Gynec. and Obst., August, 1913.
Titus, Paul: Pennsylvania Med. Jour., February, 1918.

Veil, W. H.: Arch. f. Gynäk., Berlin, 1917, pp. 107, 199.
Vinay: Bull. Médical, Aug. 24, 1907.

Walker, W. K.: New York Med. Jour., March 2, 1918.
Walter: Jour. Am. Med. Assn., April 24, 1915.
Watson, Leigh F.: Jour. Am. Med. Assn., Sept. 25, 1915.
—. Med. Rec., New York, Feb. 24, 1917.
—. Jour. Am. Med. Assn., Sept. 14, 1918.
Weber, Leonard: Med. Rec., New York, Feb. 12, 1908.
Welsh: Jour. Anat. and Phys., xxxii, 1898.
Williams, Leonard: Encyc. of Med. and Surg., London, 1912.
Wilson, L. B.: Am. Jour. Med. Sc., 1916, clii.
—. Am. Jour. Med. Sc., 1918, clvi.
Wilson, Poynton and Stoney: Proc. Roy. Soc. Med., London, 1916,
27-60, (Abstract Endocrin. ii, No. 4).
Woodbury, M. C.: Jour. Nervous and Mental Diseases, June, 1918.
Wyeth: Med. Rec., New York, May 29, 1915.

Zentmayer, Wm.: Jour. Am. Med. Assn., July 7, 1917.

INDEX

A

Abderhalden reaction in diagnosis, 143
Abdominal symptoms, 69, 174
Abortion, habitual, thyroid therapy in, 62
  in exophthalmic goiter, 181
Abortive type of Graves' disease, 115
Abrahams, R, 153
Accessory thyroid goiter, 154
    carcinoma of, 154
    diagnosis of, 155
  hyperactivity of, 32, 73, 154
  hyperplasia of, 32, 73, 154
  hyperthyroidism of, 32, 73, 154
Accidents in surgical treatment, 343
Acetonitrile poisoning and thyroid therapy, 56
Acromegaly, 76
Acute Basedow's disease, 115
  exacerbations following thyroidectomy, 116
Addisonian melanoderma, 176
Addison's disease and exophthalmic goiter, 64, 108, 176, 189
  differentiated from exophthalmic goiter, 189
Adenoids in pathogenesis, 89, 178
Adhesive plaster in treatment, 294
Adrenal discharge and splanchnic stimulation, 65
  theory in pathogenesis, 108
Adrenals, relation of, to emotions, 108
  retarded in emotions, 108
  thyroid therapy in, 64
Adrenin, increase in thyroid therapy, 64
  in treatment of vagotonia, 120
  mydriasis, 162
  test in diagnosis, 65, 127, 206
  therapy and thyroid physiology, 65
Affection in psychotherapy, 317
Age and iodine content of thyroid, 42
  and size of thyroid, 25, 59
  in course and prognosis, 215
  in pathogenesis, 86
Aikens, W. H. B., 307
Albuminuria, 184
Alexander, 196
Alt, K., 286
Ammonia furnished by thyroid, 62
Analogy of appendicitis and hyperactive thyroid, 381
  of thyroidectomy and tonsillectomy, 383
Anaphylaxis in vagus irritation, 120
Anatomical relations of parathyroids, 33
  of thyroid, 25, 26
Anatomy of thyroid, 25
  practical remarks on, 30
Anders, J. M., 115, 132, 285
Anemia, differentiated from exophthalmic goiter, 189
  erroneous diagnosis of, 117
  in exophthalmic goiter, 140, 141
Angina pectoris differentiated from exophthalmic goiter, 189
  in exophthalmic goiter, 133
Anginoid precordial pains, 33
Angioneurotic edema in exophthalmic goiter, 178
Anorexia, 173
Antidiphtheritic serum in treatment, 277
Antiseptics, intestinal, in treatment of goiter, 236
Antitoxic function of thyroid, 100, 101
Appendicitis and hyperactive thyroid, analogy of, 381
Appendix, 401
Appetite, 260
Aran, 103
Armies, neuropsychiatry in, 197
Arrhythmia, 138
Arsenic in treatment, 281
Arsimoles and Legrand, 172
Arteries, throbbing of, 139
Artificial Basedow, 87, 129, 130
Artificial exophthalmic goiter, 87, 129, 130
Asthma and exophthalmic goiter, 180
Atropin in treatment, 286
Auricular fibrillation, 138
Auscultation of thyroid, 74, 139, 147

Autotoxemic irritation of sympathetic in pathogenesis, 31, 104, 105
Autotransplantation of thyroid, 38
Azam, J., 110

B

Baber, 27
Bacigalupo, G., 298
Baily, P., 196
Balfour, D. C., 151
Ballet and Enriquez, 112
Barker, G., 105, 169
Barr, Sir J., 199, 273, 274, 286
Barry, 106
Baruch, 94
Basal metabolism and thyroxin, 45, 49, 50
    as influenced by thyroid hormone, 45, 49, 50, 63
    in cretinism, 51, 52
    in exophthalmic goiter, 59, 119, 184, 255
    test, 208
Basch, 106
Basedow, artificial, 129
  "fruste," 124
  secondary, 128
  theory in pathogenesis, 91
Basedowified accessory thyroid, 154
  cancer of thyroid, 152
  goiter, 128, 148
  goiter, iodine in treatment of, 148
  intrathoracic goiter, 154
"Basedowische Krankheit," 80
Basedow's disease, acute, 115
  as synonym of exophthalmic goiter, 80
  in soldiers, 200
Bassinger, H. R., 56
Bathing in treatment, 252
Bauman, 42
Bayer, 105, 106
Becker, 163
Béclère, 112
Beebe, S. P., 55, 97, 101, 391
Beebe and Beveridge, 59
Bell, Blair, 286
Bell, Sir Charles, 97
Belladonna in treatment, 286
Belot and Simon, 306
Bénard, C., 155
Bensley, R. R., 37
Berkley, H. J., 274, 277
Bernard, C., 103
Bernhard, 235
Bernhardt, M., 153
Berry, J., 76, 85, 389
Bialokur, 88, 153
Bibliography, 403
Billiet, 234
Bircher, 106
Bishop, H. D., 57
Blood, coagulability of, in hyperthyroidism, 58, 142
  findings as diagnostic test, 210
  findings of prognostic value, 141
  in hyperthyroidism, 58, 140, 141
  in hypothyroidism, 58
  pressure and thyroid therapy, 57, 58
  pressure, 140
  sugar in thyroid deficiency, 68
  sugar in thyroid disease, 67
  supply as influencing thyroid secretion, 37, 38
  supply of parathyroids, 33
  supply of thyroid, 28, 29, 30, 31, 36
  vessels, 138
  vessels, pulsation of, 74
Blum, 57, 95
Bodily tremor, 167
Body wasting, 119
Boggs, R., 304
Boiling water injections into thyroid, 297, 385
Bondouin and Forak, 207
Bowels, hemorrhages from, 142
  in exophthalmic goiter, 175
Bradycardia in hypothyroidism, 58
Brissaud, 74
Bromides in treatment, 287
Brooks, H., 198
Brown, O. H., 180
Bruit in thyroid enlargement, 32, 74, 139, 147
  over eye, 162
  over thyroid, 74, 139, 147
Bumstead, C. V. R., 75, 86
Burns, 31
Butler, G. R., 163

C

Caballos, A., 298
Cachexia strumipriva, 47
  in mortality of exophthalmic goiter, 214, 384
  postoperative, 384
Calcium in treatment, 272, 286
  therapy in tremor, 63
Cannon, W. B., 29, 102, 103, 108
Cannon and Cattell, 65
Capelle, 105, 106
Capillary pulse, 140

Carbohydrate tolerance, 191
Carbolic acid injections into thyroid, 295
Carcinoma in hyperplastic thyroid, 151
  of accessory thyroid goiter, 154
  of thyroid 32, 86, 151
    Basedowified, 152
    diagnosis of, 152
    frequency of, 151
    hyperthyroidism in, 152
Cardew, Denton, 176
Caro, 179
Carotid ligation in treatment, 384
Case histories of nonsurgical cures, 343
Causes, predisposing, 85
Cervical sympathetic affection in pathogenesis, 104
Charcot, 103, 178
Charcot and Marie, 164
Children, goiter in, 236
  size of thyroid in, 25, 29
Chloasma, 176
Chorea differentiated from exophthalmic goiter, 190
  in exophthalmic goiter, 171
  tremor of, 167
Chvosteck, 275
Circulation and the thyroid, 57
  effect of thyroid therapy on, 57
Circulatory system, 130
Circumference of neck, relation of, to volume of thyroid, 25
Claisse, P., 52
Cleret, 93
Climatotherapy in treatment, 227, 251
Clunet, J., 109
Coagulability of blood, 58, 142
Cobb, I. G., 56
Coenan, 119
Cohen, S. S., 64, 113, 160, 174, 177, 253, 271, 273, 274, 397
Colectomy in treatment, 237, 385
  in treatment of goiter, 237, 385
Collodion in local treatment, 294
Colloid, 39
  constituents of, 40
  in hyperplastic thyroid, 75
  proportion to activity of thyroid, 40
  proportion to thyroid secretion, 40
  quantity in thyroid, 40
Complement-fixation test as diagnostic, 210
Complications in course and prognosis, 218
Compressibility of hyperplastic thyroid, 74, 139, 147
Conclusions on nonsurgical treatment, 381
  on physiology of thyroid, 71
Confession in psychotherapy, 319
Congenital exophthalmic goiter, 127
Contraindications to operation, 395
Conversation in psychotherapy, 338
Cooperation in treatment, as influencing course and prognosis, 220
  in treatment, 231
Corneal ulceration, 161
Corpus luteum in treatment, 274
Corvisart, 195
Cough, 179
Course and prognosis, 211
  age in, 215
  blood findings in, 141
  complications in, 218
  diabetes mellitus in, 219
  digestive factors in, 216
  duration of disease in, 218
  duration of treatment in, 225
  early diagnosis in, 221
  environments in, 226
  extrinsic factors in, 221
  heart in, 217
  intrinsic factors governing, 215
  mode of treatment in, 222
  nervous system in, 217
  personality of physician in, 228
  pregnancy in, 219
  pressure symptoms in, 218
  previous health in, 215
  severity of disease in, 218
  sex in, 215
  social conditions in, 219
  tuberculosis in, 218
Course of acute Graves' disease, 115
Cramer and McCall, 68
Cream in treatment, 264
Cretinism, 47
  basal metabolism in, 51, 52
Crile, G. W., 74, 91, 92, 102, 117, 187, 246, 390
Criticisms of surgery, 200, 381
Crookshank, 55, 72
Crotti, A., 28, 41, 57, 141, 152, 234, 388, 393
Cure, apparent, 75
  case histories of, 343
  following shock (case history), 83
  nonsurgical, 343
  spontaneous, 82, 392
  surgical, 391, 398
  when attained, 211, 225, 231
Curschman, H., 163, 180

Curschman and Loewi, 162
Cutaneous symptoms, 175
Cyanosis from thyroid pressure, 32
Cyriax, R. J., 176

D

DaCosta, 195
d'Aintolo, 30
Dalrymple sign, 118, 160
D'Arsonval current in treatment, 311
Darwin, C., 97
Death, cause of, from thyroidectomy, 116
  cause of, 116, 212, 213, 214, 384
  from ligation in surgery, 384
  from thyroidectomy, 212, 213, 214
  postoperative, causes of, in treatment, 116, 117, 343, 391, 394
Dechlorination in treatment, 286
Deductions to assist in treatment, 72
Defensive function of thyroid, 101
Degeneration of thyroid, 74
DeGraefe, 103
Delille, 110
Dementia, 172
Depressor substance in blood, 143
Dermographia, 140, 177
Detoxication in thyroid physiology, 55, 100, 181
Diabetes mellitus and exophthalmic goiter, 117, 183, 190, 192, 214, 219
    dietetic treatment of, in exophthalmic goiter, 268
    differentiated from exophthalmic goiter, 190, 193
    erroneous diagnosis of, 117
    frequency of, in exophthalmic goiter, 191
    in course and prognosis, 219
    in hypothyroidism, 214
    in mortality of exophthalmic goiter, 214
    thyroidectomy in, 68
Diagnosis, differential, of exophthalmic goiter, 185
  differential, of goiter, 147
  early, in course and prognosis, 221
    in treatment, 230
  erroneous, of anemia, 117
    of diabetes mellitus, 117
    of nephritis, 117
    of nervous dyspepsia, 117
    of "nervousness," 117
    of neurasthenia, 117
    of tuberculosis, 117
  of accessory thyroid goiter, 155
Diagnosis—Cont'd.
  of carcinoma of thyroid, 152
  of exophthalmic goiter, 147, 185
    Abderhalden reaction in, 143
    basal metabolism test in, 208
    blood findings, test in, 210
    complement-fixation test in, 210
    digitalis administration in, 210
    Goetsch test in, 65, 127, 206
    hyperglycemia test in, 208
    pituitary test in, 207
    thyroid extract administration in, 209
  of "formes frustes," 125
  of secondary Basedow, 149
  of tachycardia, 135, 136
  of thymus hyperplasia, 66
Diagnostic tests in exophthalmic goiter, 206
Diaminization, physiology of thyroid, 62
Diet as affecting iodine content, 41
  in pathogenesis of goiter, 237
  iodine content of, 41
  lists in treatment, 266
Dietetic treatment, 255
    appetite in, 260
    cream in, 264
    eggs in, 257, 264
    extra nourishments in, 263, 264
    flesh foods in, 265
    gain of weight in, 258, 259, 269
    index of improvement in, 258, 259, 269
    management of digestive disorders in, 259
    milk in, 257
    nonflesh foods in, 265
    number of meals in, 262
    prescriptions for digestive disturbances in, 260
    with diabetes, 268
    with glycosuria, 268
Dieulafoy, 390
    of exophthalmos, 158, 159
    of goiter, 147
    of hyperidrosis, 176
    of hyperplastic goiter, 147
    of secondary Basedow, 149
    of simple goiter, 147
    of tachycardia, 135, 136
    of tremor, 165, 166, 167
Digestive disorders, treatment of, 259
  disturbances, prescriptions for, 260
  system in course and prognosis, 216
Digitalis administration as diagnostic test, 210
  in treatment, 286

Diphtheria intoxication and thyroid function, 56
Dryness of eyes, 162
Drysdale, H. H., 170
Du Bois, E. F., 51
Ductless gland disease and sugar tolerance, 120
Ductless glands in vagotonia, 120
Duration of disease, in course and prognosis, 218
  of treatment, 211, 225, 231
Dysphagia from goiter pressure, 32, 139, 173
  in exophthalmic goiter, 32, 139, 173
Dyspnea from goiter pressure, 32, 139, 173
  in exophthalmic goiter, 117, 134
Dysthyroidism, 123, 124
  as synonym of exophthalmic goiter, 81

E

Early diagnosis in treatment, 230
Eastman, T. B., 111
Ebstein, 285
Eclampsia, thyroid therapy in, 58, 69
Eddy, N. B., 107
Eggs in dietetic treatment, 257, 264
Ego in health and disease, 314
Electricity in treatment, 231, 299
  D'Arsonval current, 311
  galvanism, 308
  high frequency current, 310
  Leduc's current, 310
  Radium, 307
  static current, 309
  x-ray, 300
Ellis, Havelock, 59, 60
Embryology of thyroid, 34
Emotional disturbances in pathogenesis, 96
  excitement, tremor in, 165
  mentor, thyroid as, 69
Emotions and thyroid hyperactivity, 70
  heart rate in, 135, 136
  in exophthalmic goiter, 108, 170
  in thyroid physiology, 40, 69
  relation of adrenals to, 108
  thyroid secretion in, 40, 69
Endemic goiter, 85
Endocarditis differentiated from exophthalmic goiter, 190
  heart rate in, 136
Engel-Reimers, 88
Enterotoxemia theory in pathogenesis, 94, 96
Enterotoxins and thyroid physiology, 57, 94, 95
Environments in course and prognosis, 226
  social, in psychotherapy, 327
Epidemiological research in goiter, 236
Epilepsy, 170
Epiphora, 162
Epistaxis from goiter pressure, 32, 139
Eppinger and Hess, 114, 119, 120
Epstein, W., 95
Ergotin in treatment, 288
Erythrol tetranitrate in treatment, 354
Eshner, A. A., 86
Esthetic recreation in psychotherapy, 339
Etienne and Richard, 196
Etiology, 80
Etiology of exophthalmos, 157, 158, 159
Eulenberg and Panas theory in pathogenesis, 91
Exacerbations, acute, following thyroidectomy, 116
  in surgical treatment, 116, 343, 394
  postoperative, 116, 343, 394
Examination of goiter, 146
Exciting factors in pathogenesis, 91
Exercise in psychotherapy, 329
  in treatment, 249
  passive, in treatment, 251
Exophthalmic goiter, 50, 51
    abdominal symptoms in, 69, 174
    acromegaly in, 76
    acute, 115
    adenoids in, 89, 178
    albuminuria in, 184
    and Addison's disease, 64, 108, 176, 189
    and asthma, 180
    and diabetes mellitus, 117, 183, 190, 192, 214, 219
    and neurasthenia, 187
    and shell shock, 195
    and suprarenals, 64
    and tuberculosis, 88, 153, 179, 180
    anemia in, 140, 141
    angioneurotic edema in, 178
    a nonsurgical disease, 381
    anorexia in, 173
    arterial throbbing, 139
    artificial, 129

Exophthalmic goiter—Cont'd.
associated with hypothyroidism, 93, 113, 121, 123, 149
associated with tuberculosis, 88, 153, 179, 180
as synonym in hyperthyroidism, 80
auscultation of thyroid in, 74
basal metabolism in, 51, 119, 184, 255
blood in, 58, 140, 141
blood pressure in, 140
blood vessels in, 138
bodily pains in, 171
bowels in, 175
carbohydrate tolerance in, 191
carcinoma in, 86, 151
causes of death in, 212, 213, 214
chorea in, 171
circulatory system in, 130
coagulability of blood in, 58, 142
congenital, 127
cough in, 179
course and prognosis of, 211
cutaneous symptoms in, 175
dementia in, 172
dermographia in, 177
diabetes mellitus in, 117, 183, 190, 192, 214, 219
diagnosis of, 185
diagnostic tests in, 206
dietetic treatment of, 255
differential diagnosis of, 185
differentiated from Addison's disease, 189
from anemia, 189
from angina pectoris, 189
from chorea, 190
from diabetes mellitus, 190, 193
from endocarditis, 190
from hypothyroidism, 193
from hysteria, 188
from insanity, 190
from nervous indigestion, 188
from neurasthenia, 187
from paralysis agitans, 190
from psychoses, 190
from pulmonary tuberculosis, 180, 188
from secondary Basedow, 149
dyspagia in, 173
dyspnea in, 117, 134
edema in, 175
electrotherapeutic treatment of, 299
emotions in, 108, 170

Exophthalmic goiter—Cont'd.
enlargement of thymus in, 58, 66, 76, 105, 106
epilepsy in, 170
etiology of, 80
exercise in treatment of, 249
exophthalmos in, 118
experimental, 29, 30, 93, 94
eyes in, 118, 155
fecundity in, 181
gastric symptoms in, 174
gastrointestinal tract in, 69, 173
general medicinal treatment, 270
genitourinary symptoms in, 181
glycosuria in, 67, 183
goiter in, 139
gums in, 173
headache in, 171
heart failure in, 138, 213
heart in, 132
hemophilia in, 58
hemorrhages in, 142
heredity in, 71
histories of nonsurgical cures, 343
hygienic treatment of, 245
hyperglycemia in, 191
hyperidrosis in, 176
hysteria in, 171
in negroes, 87
insanity in, 172
in soldiers, 195
insomnia in, 169, 171, 183
intestinal symptoms in, 175
kinetic drive in, 92, 246
local treatment of, 291
lymphatics in, 58
mania in, 172
menstrual disturbances in, 170, 181
metabolism in, 51, 119, 184
migraine in, 171
mortality of, 116, 212, 213, 214, 384
mouth in, 173
muscular weakness in, 118
nausea in, 174
nervous symptoms in, 118, 163, 170
nervous system in, 118, 163
neurasthenia in, 171
nonsurgical treatment of, 229
nose in, 178
occurrence of goiter in, 117, 139, 143
palpitation in, 117, 132, 133
pathogenesis of, 80
pathology of, 73

Exophthalmic goiter—Cont'd.
  pathology of thyroid in, 73
  pelvic lesions in, 110, 182
  pigmentation in, 176
  pituitary therapy in, 64
  predisposition to, 96
  prognosis of, 211
  prolonged engagements in pathogenesis of, 245
  prophylaxis of, 232, 244
  psychic disturbances in, 118, 171
  psychoses in, 171
  psychotherapy in, 23, 24, 226, 311
  pulsation of blood vessels in, 74
  pulse in, 140
  recent increase of cases in, 22
  reflexes in, 171
  respiratory symptoms in, 178
  rest in treatment of, 245
  saliva in, 173
  secondary, 128
  sex in, 60, 86
  sexual disturbances in, 181
  size of thyroid in, 73
  skin in, 58, 64
  succeeded by hypothyroidism, 74, 113, 121, 123
  suprarenal therapy in, 64
  sympatheticotonic symptoms in, 121
  symptomatology of, 115
  symptoms of usual type of, 117
  tachycardia in, 117, 134
  teeth in, 173
  temperament and disposition in, 168
  temperature in, 178
  thymus enlargement in, 58, 66, 105, 106
  thymus in, 58
  thyroid enlargement in, 91, 143
  thyroid gland in, 91, 143
  thyroid hyperesthesia in, 126
  thyroid size in, 73
  thyroid therapy in, 51
  trembling in, 164
  tremor in, 118, 163
  tuberculosis in, 88, 153, 179, 180
  vagotonic symptoms of, 120
  vasomotor instability in, 58, 140, 177
  vomiting in, 174
  wasting in, 119
  without goiter, 33, 145
  x-ray treatment in, 300
Exophthalmos, 155
  causes of, 157
  degree of, 156
  development of, 155
  differential diagnosis of, 158, 159
  frequency of, in exophthalmic goiter, 155
  in angina pectoris, 158
    angioneurotic edema, 159
    antrum disease, 159
    bronchial asthma, 158
    chloromata, 159
    dyspnea, 158
    emotional excitement, 158
    exophthalmic goiter, 118
    hydrocephalus, 159
    myopia, 158
    orbital disease, 159
    paralysis of ocular muscles, 159
    stimulation of cervical sympathetic, 158
    thrombosis of superior longitudinal sinus, 158
  pulsating, 159
  sympathectomy in treatment of, 155
  thyroid therapy in, 156
  unilateral, 157
Experimental exophthalmic goiter by phrenic-sympathetic anastomosis, 103
Experimental hyperthyroidism, 94
  by transplantation, 29, 30, 93, 94
  in cat, 29, 30
Extra nourishments in dietetic treatment, formulæ for, 263, 264
Extrinsic factors in course and prognosis, 221
Eyes in exophthalmic goiter, 118, 155
  adrenalin mydriasis in, 162
  brows and lashes, falling of, 162
  bruit over, 162
  corneal ulceration, 161
  Dalrymple's sign, 118, 160
  dryness of, 162
  epiphora, 162
  feeling of pressure of, 162
  Goffre's sign, 162
  "hitch" sign of, 160
  Jellinek-Teillais sign, 162
  Kocher's sign, 161
  lachrymation, 162
  Moebius sign, 118, 160
  nystagmus, 162
  ophthalmoscopic changes, 163
  optic atrophy, 163
  panophthalmitis, 161
  reversion of Argyll Robertson pupil, 163

Eyes in exophthalmic goiter—Cont'd.
  Rosenbach's sign, 165
  Stellwag's sign, 118
  Suker's sign, 161
  tremor of, 161, 165
  vision, 163
  VonGraefe's sign, 118, 160

F

Faber, 305
Factors, extrinsic, influencing course and prognosis, 221
  intrinsic, in course and prognosis, 215
Fads in medicine, 20
Fallacy of surgery, 21, 343, 344, 381, 394
"False Basedow" from pressure on cervical sympathetic, 90, 150
    from sympathetic irritation, 90, 150
Falta, 27
Fassin, 101
Fecundity, 181
Females, size of thyroid in, 25, 29
Ferments in blood, 143
Fetal thyroid, iodine content of, 41
Fever, heart rate in, 135
Flesh foods in treatment, 265
Florez, M. Y., 85
Foods, Iodine Content of, 57
  toxicity of, 57
Forcheimer, F., 277, 279
"Formes frustes," 125, 145
  diagnosis of, 125
Formulæ in treatment of average case, 288
Frazier, C. H., 389
Freud, H., 60
Freund, 305
Friedreich's theory in pathogenesis of, 91
Fright and bodily reaction, 70
  chronic, resembling exophthalmic goiter, 70
  in pathogenesis, 96, 97
Frugoni, 101
"Fruste" form of exophthalmic goiter, 124

G

"Gallop rhythm," 138
  galvanism in treatment, 308
  galvanopalpation, 177
Garre, 105, 106
Gastaud, P., 191
Gastrointestinal hygiene in treatment, 254
  tract in exophthalmic goiter, 69, 173
  tract in thyroid insufficiency, 69
Gauthier's theory in pathogenesis, 111
Gaylord, 95, 237
Gebele, 107
Geigel, 77
Genitourinary symptoms in exophthalmic goiter, 181
Geographical distribution, 85
  location and size of thyroid, 25
  location in pathogenesis of goiter, 234
Germs in pathogenesis, 237
Geyelin, 191
Gilbert and Castaigne, 153
Gingivitis in pathogenesis, 89
Glandular equilibrium, disturbance of, 84
Glandular interdependence, 113
  interrelationship, 113
Gley, 63, 93, 109
Glycosuria, 67, 183
  dietetic treatment of, in exophthalmic goiter, 268
Goetsch, 65, 127, 206
  test in diagnosis, 65, 127, 206
Goffre's sign, 162
Goiter, Basedowified, 128
  bruit of, 147
  carcinoma of, 86, 151
  colloid in, 75
  compressibility of, 74, 139, 147
  diet in pathogenesis, 237
  differential diagnosis of, 147
  endemic, 85
  epidemiological research in, 236
  examination of, 146
  geographical location in pathogenesis, 234
  heart, Kocher's, 132, 154
  heart, mechanical, 132, 154
  heart, Rose's, 132, 154
  heredity in pathogenesis, 234
  hyperplastic, compressibility of, 74, 139, 147
  hyperplastic, differential diagnosis of, 147
  hyperplastic, tenderness of, 74, 147
  in children, 236
  in exophthalmic goiter, 139
  in pregnancy, 60
  in soldiers, 195
  intrathoracic, 154
  iodine in prophylaxis of, 238
  mobility of, 146
  nonhyperplastic, 147

Goiter—Cont'd.
  occurrence of, in exophthalmic goiter, 117, 143
  of accessory thyroid, diagnosis of, 155
  pathogenesis, microorganisms in, 237
  pathogenesis of, 233
  pressure, cyanosis from, 32
    dysphagia from, 32, 139, 173
    dyspnea from, 32, 139, 173
    epistaxis from, 32, 139
    headache from, 32, 139
    heart symptoms from, 132
    on larynx, 179
    on parathyroids, 63
    syncope from, 139
    vertigo from, 32, 139
    voice alterations from, 139, 179
  prevention of, 232
  primary hyperplastic, 143
  prophylactic treatment of, iodine in water, 235
  prophylaxis of, 232
  regeneration, postoperative, 343
  sex in pathogenesis of, 234
  shape of, 146
  simple, 147
  simple, differential diagnosis of, 147
  throbbing of, 146
  transplantation, 29, 30, 93, 94
  water in pathogenesis of, 234
Gonad theory in pathogenesis of exophthalmic goiter, 110
Gordon, M. B., 106
Gottlieb, 93
Grafting of thymus with Basedowian syndrome, 106
Grafts, thyroid, 38
Graves, 80
Graves' disease, 50, 51
  abdominal symptoms in, 69, 174
  acromegaly in, 76
  acute, 115
  adenoids in, 89, 178
  albuminuria in, 184
  and Addison's disease, 64, 108, 176, 189
  and asthma, 180
  and diabetes mellitus,, 117, 183, 190, 192, 214, 219
  and neurasthenia, 187
  and shell shock, 195
  and suprarenals, 64
  and tuberculosis, 88, 153, 179, 180
  anemia in, 140, 141
  angioneurotic edema in, 178
Graves' disease—Cont'd.
  a nonsurgical disease, 381
  anorexia in, 173
  arterial throbbing in, 139
  artificial, 129
  associated with hypothyroidism, 93, 113, 121, 123, 149
  associated with tuberculosis, 88, 153, 179, 180
  as synonym of exophthalmic goiter, 80
  auscultation of thyroid in, 74
  basal metabolism in, 51, 255
  blood in, 58, 140, 141
    pressure in, 140
    vessels in, 138
  bodily pains in, 171
  bowels in, 175
  carbohydrate tolerance in, 191
  carcinoma in, 86, 151
  causes of death in, 212, 213, 214
  chorea in, 171
  circulatory system in, 130
  coagulability of blood in, 58, 142
  congenital, 127
  cough in, 179
  course and prognosis of, 211
  cutaneous symptoms in, 175
  dementia in, 172
  dermographia in, 177
  diabetes mellitus in, 117, 183, 190, 192, 214, 219
  diagnosis of, 185
  diagnostic tests in, 206
  dietetic treatment of, 255
  differential diagnosis of, 185
  differentiated from Addison's disease, 189
    from anemia, 189
    from angina pectoris, 189
    from chorea, 190
    from diabetes mellitus, 190, 193
    from endocarditis, 190
    from hypothyroidism, 193
    from hysteria, 188
    from insanity, 190
    from nervous indigestion, 188
    from neurasthenia, 187
    from paralysis agitans, 190
    from psychoses, 190
    from pulmonary tuberculosis, 180, 188
    from secondary Basedow, 149
  dysphagia in, 173
  dyspnea in, 117, 134
  edema in, 175

Graves' disease—Cont'd.
  electrotherapeutic treatment of, 299
  emotions in, 108, 170
  enlargement of thymus in, 58, 66, 76, 105, 106
  epilepsy in, 170
  etiology of, 80
  exercise in treatment of, 249
  exophthalmos in, 118
  experimental, 29, 30, 93, 94
  eyes in, 118, 155
  fecundity in, 181
  gastric symptoms in, 174
  gastrointestinal tract in, 69, 173
  general medicinal treatment, 270
  genitourinary symptoms in, 181
  glycosuria in, 67, 183
  goiter in, 139
  gums in, 173
  headache in, 171
  heart failure in, 138, 213
  heart in, 132
  hemophilia in, 58
  hemorrhages in, 142
  heredity in, 71
  histories of nonsurgical cures, 343
  hygienic treatment of, 245
  hyperglycemia in, 191
  hyperidrosis in, 176
  hysteria in, 171
  in negroes, 87
  insanity in, 172
  in soldiers, 195
  insomnia in, 169, 171, 183
  intestinal symptoms in, 175
  kinetic drive in, 92, 246
  local treatment of, 291
  lymphatics in, 58
  mania in, 172
  menstrual disturbances in, 181
  metabolism in, 51, 119, 184
  migraine in, 171
  mortality of, 116, 212, 213, 214, 384
  mouth in, 173
  muscular weakness in, 118
  nausea in, 174
  nervous symptoms in, 118, 163, 170
  nervous system in, 118, 163, 170
  neurasthenia in, 171
  nonsurgical treatment of, 229
  nose in, 178
  occurrence of goiter in, 117, 139, 143
  palpitation in, 117, 132, 133
  pathogenesis of, 80

Graves' disease—Cont'd.
  pathology of, 73
  pathology of thyroid in, 73
  pelvic lesions in, 110, 182
  pigmentation in, 176
  pituitary therapy in, 64
  predisposition to, 96
  prognosis of, 211
  prolonged engagements in pathogenesis of, 245
  prophylaxis of, 232, 244
  psychic disturbances in, 118, 171
  psychoses in, 171
  psychotherapy in, 23, 24, 226, 311
  pulsation of blood vessels in, 74
  pulse in, 140
  recent increase of cases, 22
  reflexes in, 171
  respiratory symptoms in, 178
  rest in treatment of, 245
  saliva in, 173
  secondary, 128
  sex in, 60, 86
  sexual disturbances in, 181
  size of thyroid in, 73
  skin in, 58, 64, 175
  succeeded by hypothyroidism, 74, 113, 121, 123
  suprarenal therapy in, 64
  sympatheticotonic symptoms in, 121
  symptomatology of, 115
  symptoms of usual type, 117
  tachycardia in, 117, 134
  teeth in, 173
  temperament and disposition in, 168
  temperature in, 178
  thymus enlargement in, 58, 66, 105, 106
  thyroid enlargement in, 91, 143
  thyroid gland in, 91, 143
  thyroid hyperesthesia in, 126
  thyroid size in, 73
  thyroid therapy in, 51
  trembling in, 164
  tremor in, 118, 163
  tuberculosis in, 88, 153, 179, 180
  vagotonic symptoms of, 120
  vasomotor instability in, 58, 140, 177
  vomiting in, 174
  wasting in, 119
  without goiter, 33, 145
  x-ray treatment in, 300
Graves' theory in pathogenesis of exophthalmic goiter, 91
Greenfield, W. E., 112

Gries, G. W., 304
Grixoni, 101
Gruss, 159
Gudernatsch, J. F., 48, 106
Gums in exophthalmic goiter, 89, 173
Günzel, 310
Güttinger, 235
Gynecology in exophthalmic goiter, 183
  in treatment of exophthalmic goiter, 111

H

Haeberlin, J. B., 39
Hair and nails, 178
Hallion, 110,
Halsted, 106, 283
Halsted and Hertoghe, 95
Harmony, mental and physical, in treatment, 380
Harrower, H. R., 170, 209
Hart, 105
Hasty generalization in treatment, 395
Headache from goiter pressure, 32, 139, 171
Health, previous, in course and prognosis, 215
Heart disease, thyroid extract in, 57
  failure, 138, 213
  failure in mortality of exophthalmic goiter, 213
  in course and prognosis, 217
  in exophthalmic goiter, 132
  influence of thyroid on, 58
  in nicotine poisoning, 201
  palpitation, in exophthalmic goiter, 117, 132, 133
  pathology of, 78
  physical examination of, 137
  rate in anemias, 136
    in emotions, 135, 136
    in endocarditis, 136
    in exophthalmic goiter, 135
    in fever, 135
    in hysteria, 135
    in neurasthenia, 135
    in paroxysmal tachycardia, 136
    in "shell shock," 135
    in toxemia, 136
  subjective symptoms of, 132
  symptoms from goiter pressure, 132
    objective, in exophthalmic goiter, 134
Hedinger, 77, 106
Heidenreich, 60
Hemophilia in hyperthyroidism, 58
Hemorrhages from bowels, 142
  from lungs, 142
  from nose, 142
  from stomach, 142
  in exophthalmic goiter, 142
  postpartum, in exophthalmic goiter, 182
Hereditary influence on size of thyroid, 25
  tremor, 167
  in pathogenesis of exophthalmic goiter, 85
  in pathogenesis of goiter, 234
Hernaman-Johnson, 300
Hernaman-Johnson and White, 200
Herring, E., 64, 162
Hertzler, 110
High frequency current in treatment, 310
High-strung temperaments in pathogenesis, 96
Hirschl, 305
Hirst, B. C., 215
Histology of thyroid, 27, 28
Histories (case) of nonsurgical cures, 343
"Hitch" sign of eyes, 160
Hofbauer, L., 180
Hollervorden, 87
Home treatment, 227, 247
Homicidal tendencies, 170
Hoppe, H. H., 274
Hoskins, E. R., 64, 67
Hospital treatment, 226, 227, 247
Hunt, R., 56
Hunziker, H., 240
Hurst, A., 197
Huschke and Krause, 59
Hydrotherapy in treatment, 252
Hygiene, gastrointestinal, in treatment, 254
  mental, in treatment, 254
Hygienic treatment, 245
Hyoscine in treatment, 287
Hyperactivity of accessory thyroids, 32
Hyperglycemia, 142, 191
Hyperglycemic test, 208
Hyperidrosis in exophthalmic goiter, 176
  in exophthalmic goiter, differential diagnosis of, 176
Hyperplasia of accessory thyroid, 32, 73, 154
  of thymus, diagnosis of, 66
  of thyroid as cause of exophthalmic goiter, 74

Hyperplastic thyroid, 73, 138, 143
  bruit of, 74, 139, 147
  colloid in, 75
  compressibility of, 74, 139, 146
  differential diagnosis of, 147
  mobility, 146
  occurrence of goiter in, 143, 145
  pathology of, 73
  pulsation, 74, 138, 139, 146
  shape of, 73, 146
  size of, 73, 117, 146
  tenderness of, 74, 139, 147
  thrill of, 74, 139, 147
  throbbing of, 74, 138, 139, 146
Hyperthyroidism, 50, 51
  abdominal symptoms in, 69, 174
  acromegaly in, 76
  acute, 115
  adenoids in, 89, 178
  albuminuria in, 184
  and Addison's disease, 64, 108, 176, 189
  and asthma, 180
  and diabetes mellitus, 117, 183, 190, 192, 214, 219
  and neurasthenia, 187
  and shell shock, 195
  and suprarenals, 64
  and tuberculosis, 88, 153, 179, 180
  anemia in, 140, 141
  angioneurotic edema in, 178
  a nonsurgical disease, 381
  anorexia in, 173
  arterial throbbing in, 139
  artificial, 129
  associated with hypothyroidism, 93, 113, 121, 123, 149
  associated with tuberculosis, 88
  as synonym of exophthalmic goiter, 80
  auscultation of thyroid in, 74
  basal metabolism in, 51, 255
  blood in, 58, 140, 141
    pressure in, 140
    vessels in, 138
  bodily pains in, 171
  bowels in, 175
  carbohydrate tolerance in, 191
  carcinoma in, 86, 151
  causes of death in, 212, 213, 214
  chorea in, 171
  circulatory system in, 130
  coagulability of blood in, 58, 142
  congenital, 127
  cough in, 179
  course and prognosis of, 211
  cutaneous symptoms in, 175
  dementia in, 172
Hyperthyroidism—Cont'd.
  dermographia in, 177
  diabetes mellitus in, 117, 183, 190, 192, 214, 219
  diagnosis of, 185
  diagnostic tests in, 306
  dietetic treatment of, 255
  differential diagnosis of, 185
  differentiated from Addison's disease, 189
    from anemia, 189
    from angina pectoris, 189
    from chorea, 190
    from diabetes mellitus, 190, 193
    from endocarditis, 190
    from hypothyroidism, 193
    from hysteria, 188
    from insanity, 190
    from nervous indigestion, 188
    from neurasthenia, 187
    from paralysis agitans, 190
    from psychoses, 190
    from pulmonary tuberculosis, 180, 188
    from secondary Basedow, 149
  dysphagia in, 173
  dyspnea in, 117, 134
  edema in, 175
  electrotherapeutic treatment of, 299
  emotions in, 108, 170
  enlargement of thymus in, 58, 66, 76, 105, 106
  epilepsy in, 170
  etiology of, 80
  exercise in treatment of, 249
  exophthalmos in, 118
  experimental, 29, 30, 93, 94
  eyes in, 118, 155
  fecundity in, 181
  gastric symptoms in, 174
  gastrointestinal tract in, 69, 173
  general medicinal treatment, 270
  genitourinary symptoms in, 181
  glycosuria in, 67, 183
  goiter in, 139
  gums in, 173
  headache in, 171
  heart failure in, 138, 213
  heart in, 132
  hemophilia in, 58
  hemorrhages in, 142
  heredity in, 71
  histories of nonsurgical cures, 343
  hygienic treatment of, 245
  hyperglycemia in, 191
  hyperidrosis in, 176
  hysteria in, 171

Hyperthyroidism—Cont'd.
  in negroes, 87
  insanity in, 172
  in soldiers, 195
  insomnia in, 169, 171, 183
  intestinal symptoms in, 175
  kinetic drive in, 92, 246
  local treatment of, 291
  lymphatics in, 58
  mania in, 172
  menstrual disturbances in, 181
  metabolism in, 51, 119, 184
  migraine in, 171
  mortality of, 116, 212, 213, 214, 384
  mouth in, 173
  muscular weakness in, 118
  nausea in, 174
  nervous symptoms in, 118, 163, 170
  nervous system in, 118, 163, 170
  neurasthenia in, 171
  nonsurgical treatment of, 229
  nose in, 178
  occurrence of goiter in, 117, 139, 143
  of accessory thyroid, 154
  palpitation in, 117, 132, 133
  pathogenesis of, 80
  pathology of, 73
  pathology of thyroid in, 73
  pelvic lesions in, 110, 182
  pigmentation in, 176
  pituitary therapy in, 64
  predisposition to, 96
  prognosis of, 211
  prolonged engagements in pathogenesis of, 245
  prophylaxis of, 232, 244
  psychic disturbances in, 118, 171
  psychoses in, 171
  psychotherapy in, 23, 24, 226, 311
  pulsation of blood vessels in, 74
  pulse in, 140
  recent increase of cases, 22
  reflexes in, 171
  respiratory symptoms in, 178
  rest in treatment of, 245
  saliva in, 173
  secondary, 128
  sex in, 60, 86
  sexual disturbances in, 181
  size of thyroid in, 73
  skin in, 58, 64
  succeeded by hypothyroidism, 74, 113, 121, 123
  suprarenal therapy in, 64
  sympatheticotonic symptoms in, 121
  symptomatology of, 115

Hyperthyroidism—Cont'd.
  symptoms of usual type, 117
  tachycardia in, 117, 134
  teeth in, 173
  temperament and disposition in, 168
  temperature in, 178
  theory in pathogenesis, 111
  thymus enlargement in, 58, 66, 105, 106
  thymus in, 58
  thyroid enlargement in, 91, 143
  thyroid gland in, 91, 143
    hyperesthesia in, 126
    size in, 73
    therapy in, 51
  trembling in, 164
  tremor in, 118, 163
  tuberculosis in, 88, 153, 179, 180
  vagotonic symptoms of, 120
  vasomotor instability in, 58, 140, 177
  vomiting in, 174
  wasting in, 119
  without goiter, 33, 145
  x-ray treatment in, 300
Hypothyroidism, 47, 48
  associated with hyperthyroidism, 93, 113, 121, 123, 149
  blood in, 58
  bradycardia in, 58
  diabetes mellitus in, 214
  differentiated from hyperthyroidism, 193
  experimental, 93
  skin in, 58
  succeeding hyperthyroidism, 74, 113, 121, 123
Hysteria, differentiated from exophthalmic goiter, 188
  heart rate in, 135
  in exophthalmic goiter, 171
  tremor in, 166

I

Ice bags in treatment of exophthalmic goiter, 252, 294
Ichthyol in treatment, 288
Idleness in psychotherapy, 329
Inconsistency of surgery, 382
Indecision of surgeons in treatment, 384
Indications for surgery, 229, 230, 381, 386
Individualization in treatment, 231, 270, 380
Infections in pathogenesis, 88
  in thyroid physiology, 40
  thyroid secretion in, 40

Injections of boiling water into thyroid, 297
  of carbolic acid into thyroid gland, 295
  of iodine into thyroid gland, 153, 282, 295
  of quinine and urea into thyroid, 295, 296, 385
Insanity differentiated from exophthalmic goiter, 190
  in exophthalmic goiter, 172
  in mortality of exophthalmic goiter, 213
Insomnia in exophthalmic goiter, 169, 171, 183
Inspection of hyperplastic thyroid, 74
Instinct of self-preservation in emergencies, 71
Intercurrent affections in mortality of exophthalmic goiter, 214
Interglandular epuilibrium, 62
Internists' opinions on treatment, 396
Intestinal antiseptics in treatment, 236, 285
  symptoms in exophthalmic goiter, 175
Intoxications, tremor in, 165
Intrathoracic goiter, 154
  goiter, Basedowified, 154
Intrinsic factors in course and prognosis, 215
Introduction, 17
Iodides in treatment, 148, 153, 213, 282, 292, 295
Iodine-Basedow, 87, 129, 130
Iodine content as affected by diet, 41
    of diet, 41, 57
    of fetal thyroid, 41
    of foods, 41, 57
    of goitrous thyroid, 41
    of thyroid, 41
    of thyroid, age in, 42
    of thyroid in parturition, 41
    of thyroid in pregnancy, 41
    of thyroid, residence in, 42
    of thyroid, sex in, 42
    seasonal variations of, 41, 42
Iodine injections into thyroid gland, 295
Iodine in local treatment, 292
  in pathogenesis, 87
  in prophylaxis of goiter, 235, 238
  in thyroid autotransplantation, 38
  in treatment of Basedowified goiter, 148
  in treatment of exophthalmic goiter, 87, 153, 213, 282, 295
Iodine—Cont'd.
  in water in prophylactic treatment of goiter, 235
  quantity of, in tissues, 41
Iodothyrin, 42
Iodothyroglobulin, 42
Iron in treatment, 281
Irritability of patients, 169
Iscovesco, 93
Isthmus of thyroid, 26

J

Jaboulay, 105, 155
Jackson, J. M., 288
James, Wm., 339
Janney, N. W., 112, 123, 208
Janney and Isaacson, 67
Janney's theory in pathogenesis, 112
Jellinck-Teillais, eye sign, 162
Joffroy's test, 178
Jonesco, 155

K

Kahane, 177
Kaplan, D. M., 53
Kappenburg, B. D. G., 172
Kendall, E. C., 43, 44, 45, 46, 49, 62
Kidneys, relation of thyroid to, 69
Kinetic drive in exophthalmic goiter, 92, 246
Kinetic system, 92
    activators of, 92
Kjlstad, S., 241
Klinger, P., 240
Klose, 94
Knopf, A. S., 88, 152
Kocher, A., 76, 93, 105, 117, 141, 162, 235
Kocher's goiter heart, 132
  sign, 161
Koeben's theory in pathogenesis, 103, 104
Kojima, M., 67
Kraus, 143
Krummer, E., 38, 39
Kuriyama, 68

L

Lachrymation in exophthalmic goiter, 162
Lactation, thyroid size in, 60
  thyroid therapy in, 61
Lactic acid ferments in treatment, 275
Lambert, 101
Lampa and Deutsch, 143
Lampé, 94

Lampé and Klose theory in pathogenesis, 112
Landrom, 157
Lane, Sir Arbuthnot, 58, 95, 237, 385
Lanz, O., 277, 282
Larynx, compression of, 179
Laughter in psychotherapy, 330
Lecithin in treatment, 277
Lectures in psychotherapy, 337
Lédoux-Lébard, 300
Leduc's current in treatment, 310
Leiter coils in treatment, 252, 253
Levator Glandulæ Thyroidiæ, 27
Lévi, Léopold, 121
Lévi and Rothschild, 123
Levy, 65
Lewis, Dean, 390
Lian, 126
Lichty, J. A., 255
Liesegang, 94
Ligation, death from, 384
Ligations in treatment, 343, 384
Liver and thyroid physiology, 68
Lloyd, J. H., 115
Local treatment, 291
  adhesive plaster in, 294
  carbolic acid injections in thyroid, 295
  collodion in, 294
  ice caps in, 252, 294
  injections into thyroid, 295
  injections of boiling water into thyroid, 297
  iodine injections into thyroid, 295
  prescriptions in, 293
  quinine and urea injections into thyroid, 296
  salt bags in, 294
  sand bags in, 294
Lorand, C. R., 114
Love in psychotherapy, 321
Lucien, M., 109
Lugaro, 101
Lungs, hemorrhages from, 142
Lymphatics in hyperthyroidism, 58
  of thyroid gland, 29

M

MacCallum, W. G., 77
MacDonnel and Moore, 77
Mackenzie, Hector, 76, 86, 97, 106, 273
Mackinnon, R., 78
Males, size of thyroid in, 25, 29
Malignancy of thyroid, 32, 86, 151
Malignant changes in hyperplastic goiter, 32, 86, 151
Maloney, W. J. M. A., 252
Mania in exophthalmic goiter, 172
Manley and Marine, 38
Mann, 101
Marbé, 101
Maria, Santa, 179
Marie, Pierre, 80, 112, 148
Marimon's theory in pathogenesis, 92
Marine, D., 41, 59, 74
Marine and Graham, 74
Marine and Kimball, 233, 238, 240
Marine and Lenhart, 76, 142, 158, 283
Markoe, J. W., 298
Marsh, Pral, Maumann and Hensinger theory in pathogenesis, 91
Matti, 106
Maurice, 158
Mayo, Chas. H., 28, 36, 44, 45, 157, 298, 299, 390
Mead, L. G., 288
Meals, number of, in treatment, 262
Means and Aub, 51, 208
Mechanical goiter heart, 154
Meckel, 59
Medical fads, 20
Medicinal general treatment, 270
Melchior, E., 66
Menopause and thyroid physiology 61
  succeeded by symptoms of exophthalmic goiter, 110
Menstrual disturbances in exophthalmic goiter, 181
Menstruation, size of thyroid in, 25, 60
  thyroid secretion in, 39
Mental depression in exophthalmic goiter, 170, 181
  disturbances in "shell shock," 99
  equanimity of patients in psychotherapy, 340
  hygiene in treatment, 254
Mentality of female and the thyroid, 59
Mental stimulation, in exophthalmic goiter, 169
  strain in pathogenesis, 96
  suggestion in psychotherapy, 340
Mercury in treatment, 281
  in treatment of syphilis of thyroid, 153
Metabolism and thyroid physiology, 47
  basal, in exophthalmic goiter, 51, 119, 184, 255
Microorganisms in pathogenesis, 237
Microscopic pathology of hyperplastic thyroid, 75, 77
Micturition, frequent, in exophthalmic goiter, 183

Migraine, 171
Milk in dietetic treatment, 257
Mind in medicine, 312
Mingus, E., 294
Miscellaneous nervous phenomena, 118, 170
Mishaps in surgical treatment, 343
Mitchell, S. Weir, 319
Mobility of goiter, 146
Moebius, O., 80, 277
Moebius sign in exophthalmic goiter, 118, 160
  theory, criticism of, 112
  theory in pathogenesis, 111
Moon and Roussel, 201
Mors thymica, 66
Mortality of exophthalmic goiter, 212, 213, 214
  cachexia strumipriva in, 214, 384
  diabetes mellitus in, 214
  heart failure in, 213
  insanity in, 213
  intercurrent affections in, 214
  myxedema in, 214
  tetany in, 214
  tuberculosis in, 213
Mortality rate in surgery, 116, 117, 343, 391, 394
Mouth and throat infections in pathogenesis, 88, 89, 100
Mouth in exophthalmic goiter, 173
Multiple sclerosis, tremor in, 167
Murmur of thyroid, 32, 74, 139, 147
Muscular weakness, 118
Music in psychotherapy, 334
Musser, 396
Myxedema, 47
  in mortality of exophthalmic goiter, 214
  postoperative, 343, 384, 395
  sex in, 60

Mc

McCarrison, R., 25, 29, 30, 31, 40, 42, 73, 94, 95, 97, 143, 163, 212, 214, 233, 236, 237, 242, 275, 282, 285, 389, 398
McCaskey, G. W., 208
McCord and Marinus, 48

N

Nasal polyps in pathogenesis, 89, 178
  sinusitis in pathogenesis, 89
Nausea in exophthalmic goiter, 174
Negroes, exophthalmic goiter in, 87
Nephritis, erroneous diagnosis of, in exophthalmic goiter, 117
  thyroid therapy in, 69
Nerve sedatives in treatment, 287
  supply of parathyroids, 33
  supply of thyroid, 29, 30, 37
Nervous disturbances in exophthalmic goiter, 118, 170
  dyspepsia, erroneous diagnosis of, in exophthalmic goiter, 117
  indigestion differentiated from exophthalmic goiter, 188
  phenomena, miscellaneous, in exophthalmic goiter, 118, 163, 170
  symptoms in exophthalmic goiter, 163
  system in course and prognosis, 217
  system in exophthalmic goiter, 118, 163, 170
  system, pathology, 77
  system, sympathetic, stimulation of, 31
  weakness in pathogenesis, 96
"Nervousness," erroneous diagnosis of, 117
Nervousness of patients, 169
Neurasthenia and exophthalmic goiter, 187
  differentiated from exophthalmic goiter, 187
  erroneous diagnosis of, 117
  heart rate in, 135
  in exophthalmic goiter, 171
  tremor in, 166
  neurocirculatory asthenia, 196
Neurogenic theory in pathogenesis, 96
Neuropathic tendency in pathogenesis, 85
Neuropsychiatry in armies, 197
Ney, K. W., 201
Nicotine poisoning as cause of irritable heart, 201
Nomenclature of exophthalmic goiter, 80, 81
Nonflesh foods in treatment, 265
Nonhyperplastic goiter, 147
Nonsurgical cures of exophthalmic goiter, case histories of, 343
  nature of exophthalmic goiter, 387
  treatment cures exophthalmic goiter, 399
  treatment, conclusions on, 381
Nordentoft, S., 301
Nordman, 105
Nose, hemorrhages from, 142
Nose in exophthalmic goiter, 178
  polyps, 178

Nourishments, extra, in treatment, 263, 264
Nux vomica in treatment, 287
Nystagmus in exophthalmic goiter, 162

O

Objections to surgery in treatment, 21, 343, 344, 381, 394
Objective heart symptoms in exophthalmic goiter, 134
Obsessions, 170
Ochsner, A. J., 393
O'Day, J. C., 157
Oesterreicher, 86
Oil injections in treatment, 285
Operations in treatment, 384
Ophthalmoscopic changes, 163
Opinions of internists in treatment, 396
Opinions of surgeons in treatment, 387
Optic atrophy, 163
Orbits, pathology of, 78
Organotherapy in treatment, 270
Oswald, A., 42
Ott and Scott, 64
Ovarian extract in treatment, 274
Ovaries in thyroid physiology, 111

P

Pains, bodily, in exophthalmic goiter, 171
Pal, 272
Palpitation, 117, 132, 133
  relation to tachycardia, 133
Pancreas and thyroid, 67
  pathology of, 78
Pancreatic extract in treatment, 275
  function inhibited by thyroid, 67
Panophthalmitis, 161
Paralysis agitans differentiated from exophthalmic goiter, 190
  tremor in, 166
Paralysis of vocal cords in surgical treatment, 31, 343, 395
Parasympathetic stimulation in vagotonia, 121
Parathyroid extract in treatment, 271
Parathyroid glands, 33
    anatomical relation of, 33
    blood supply of, 33
    interaction with thyroid, 63
    nerve supply of, 33
    pathology, 76
    removal in surgical treatment, 343, 384
    structure of, 33
Parathyroid glands—Cont'd.
    theory in pathogenesis, 109
    therapy in tremor, 63
    thyroid function, 63
    thyroid pressure on, 63
    thyroid insufficiency, 63
Parisot, J., 109, 110
Paroxysmal tachycardia, heart rate in, 136
Parry, Caleb, 80
Parry's disease as a synonym of exophthalmic goiter, 80
Parturition, iodine content of thyroid in, 41
  thyroid size in, 60
Passive exercise in treatment, 251
Pathogenesis of exophthalmic goiter, 80
    adenoids in, 89, 178
    age in, 86
    autotoxemic irritation of sympathetic in, 105
    cervical sympathetic affection in, 104
    emotional disturbances in, 96
    exciting factors in, 91
    fright in, 96, 97
    gingivitis in, 89, 173
    gonad theory in, 110
    heredity in, 85
    high-strung temperament in, 96
    infections in, 88
    iodine in, 87
    kinetic drive in, 92, 246
    mental strain in, 96
    microorganisms in, 237
    mouth and throat infections in, 88, 89, 100
    mouth infections in, 88, 100
    nasal polyps in, 89, 178
    nervous weakness in, 96
    neuropathic tendency in, 85
    nose in, 178
    pelvic lesions in, 110, 182
    prolonged engagements in, 245
    race in, 87
    sex in, 60, 86
    shock in, 97
    simple goiter in, 90
    sinusitis in, 89
    suprarenals in, 64
    sympathetic (cervical) irritation in, 104
    syphilis in, 88
    theory of Basedow in, 91
      of Eulenberg and Panas in, 91
      of Friedreich in, 91

- Pathogenesis—Cont'd.
    - of Gauthier, in, 111
    - of Gauthier and Moebius in, 91
    - of Graves in, 91
    - of Janney in, 112
    - of Koeben in, 103, 104
    - of Koeben, Aran, Trousseau and Charcot in, 91
    - of Lampé and Klose in, 112
    - of Marimon in, 92
    - of Marsh, Pral, Maumann and Hensinger in, 91
    - of Mobius in, 111
    - of Renaut in, 111
    - of Roussy in, 104
    - of Sajous in, 102
    - of Stokes in, 91
    - of Tedeschi and Warburton in, 91
  - theory, adrenal in, 108
    - enterotoxemic in, 94, 96
    - gonad in, 110
    - hyperthyroidism in, 111
    - neurogenic in, 96
    - parathyroid in, 109
    - pituitary in, 109
    - pluriglandular in, 113
    - sympathetic in, 103
    - thymus in, 105
  - thyroiditis in, 90, 150, 151
  - tonsillar diseases in, 89
  - toxemia in, 100
  - traumatism in, 90, 96, 97
  - tuberculosis in, 88
  - war conditions in, 197
  - of goiter, 233
    - diet in, 237
    - geographical location in, 234
    - germs in, 237
    - heredity in, 234
    - sex in, 234
    - water in, 234
- Pathology of exophthalmic goiter, 73
  - heart in, 78
  - hyperplastic thyroid, 75, 77
    - atypical specimens, 76
    - microscopic, 75, 77
  - nervous system in, 77
  - orbits in, 78
  - pancreas in, 78
  - parathyroids in, 76
  - pituitary in, 76
  - spleen and lymphatics in, 78
  - suprarenals in, 77
  - thymus in, 76
  - thyroid in, 73
  - tonsils and adenoids in, 79
- Pelvic disease, thyroid extract in,
  - thyroid in, 60, 61
- Pelvic lesions in pathogenesis of ophthalmic goiter, 110, 1
- Personality of physician in co and prognosis, 228
- Personality of physician in psy therapy, 325
- Petechiæ in exophthalmic goiter,
- Pettavel, 77
- Pfahler, George, 306
- Pfahler, and Zulick, 301
- Pfeiffer, 93
- Phobias, 170
- Phosphorus supply regulated by mus, 67
- Phrenic-sympathetic anastomosis syndrome of exophth goiter, 103
- Physical examination of goiter,
  - heart in, 137
- Physician's task in psychotherap exophthalmic goiter, 34
- Physiological thyroid hyperacti 61
  - thyroid swelling, 144
- Physiology of thyroid gland, 36
  - and adrenin therapy, 65
  - and circulation, 57, 130
  - and enterotoxins, 57, 94, 9
  - and gastrointestinal tract,
  - and kidneys, 69
  - and liver, 68
  - and metabolism, 47
  - and pancreas, 67
  - and parathyroids, 63
  - and sexual development, 5
  - and skin, 58, 64, 175
  - and thymus, 65
  - antitoxin, 100, 101
  - conclusions on, 71
  - defensive, 55, 100, 181
  - detoxication in, 55
  - diaminization, 62
  - diphtheria intoxication in,
  - emotional mentor, 69
  - emotions in, 40, 69
  - in infections, 40
  - in menopause, 61
  - in pregnancy, 57
  - ovaries in, 111
  - pituitary in, 64
- Piersol, George A., 30, 35
- Pietrowicz, S. R., 275
- Pigmentation in exophthalmic 64, 176
- Pisani, O., 274

Pituitary enlargement in exophthalmic goiter, 110
  in experimental thyroidectomy, 109 109
  in thyroid physiology, 64
    pathology, 76
    test in diagnosis, 207
    theory in pathogenesis, 109
  vasoconstricting influence of, 109
Pituitrin in treatment, 64, 110, 272
Plethoric features in exophthalmic goiter, 142
Plummer, 45, 50, 74, 101, 128, 151, 221
Pluriglandular nature of exophthalmic goiter, 72, 83, 84, 383
  theory in pathogenesis, 113
Polyps, nasal, in exophthalmic goiter, 89, 178
Polyuria in exophthalmic goiter, 183
Porter, M. F., 297, 389
Postoperative cachexia strumipriva, 384
Postoperative death, causes of in treatment, 116, 117, 343, 391, 394
  exacerbations in treatment, 116, 343, 394
  myxedema, 384, 395
  recurrences in treatment, 343, 344, 384, 391, 394
  regeneration of goiter, 343
  status lymphaticus, 343, 395
  tetany, 343, 384
  treatment, 393
  vocal paralysis, 31, 343, 395
Postpartum hemorrhage in exophthalmic goiter, 182
Pottenger, F. M., 119, 121
Preble, R. B., 162
Predisposing causes of exophthalmic goiter, 85
Predisposition to exophthalmic goiter, 96
Pregnancy and thyroid physiology, 57
  during nonsurgical treatment, 380
  goiter in, 60
  in course and prognosis, 219
  iodine content of thyroid in, 41
  occurrence of, in exophthalmic goiter, 181
  size of thyroid in, 25, 60, 182
  swelling of thyroid in, 25, 60, 182
  thyroid secretion in, 39
Prescriptions in local treatment, 293
  in treatment of average case, 288
Pressure of cervical vessels by goiter, 31
  goiter cyanosis from, 32
    dysphagia from, 32 139, 173
    dyspnea from, 32, 139, 173
    epistaxis from, 32, 139
    headache from, 32, 139
    heart symptoms from, 132
    on larynx, 179
    on parathyroids, 63
    syncope from, 139
    vertigo from, 32, 139
    voice alteration from, 139, 179
  symptoms in course and prognosis, 218
  of goiter, 32, 139
Prevention of goiter, 232
Prognosis of exophthalmic goiter, 211
Prognostic value of blood findings, 141
  coagulability of blood, 142
Prolonged engagements in pathogenesis of exophthalmic goiter, 245
Prophylaxis of exophthalmic goiter, 232
Prophylaxis of goiter, 232
  iodine in, 235, 238
  iodine in water, 235
Pruritis in exophthalmic goiter, 177
Psychic disturbances in exophthalmic goiter, 118, 170, 171
Psychoses differentiated from exophthalmic goiter, 190
Psychotherapy in treatment of exophthalmic goiter, 23, 24, 226, 311
  affection and sympathy in, 317
  confession in, 319
  conversation in, 338
  correction of social environments, 327
  doctor's task in, 341
  ego in, 314
  esthetic recreation in, 339
  exercise in, 249
  idleness in, 329
  individualization in, 320
  influence of body on mind, 313
  influence of mind on body, 312
  laughter in, 330
  lectures in, 338
  love in, 321
  maintenance of patient's mental equanimity, 339
  mental suggestion in, 340
  mind in medicine, 312
  music in, 334

Psychotherapy—Cont'd.
  personality of physician in, 325
  reading in, 327
  rest and exercise in, 329
  selfhood in, 315
  sexual instinct and balance, 321
  social environments in, 327
  sympathy and affection, 317
  temperament in, 315
Puberty, thyroid size in, 60
Pulmonary tuberculosis differentiated from exophthalmic goiter, 180, 188
Pulsation in thyroid enlargement, 32, 74, 139
Pulsation of vessels in exophthalmic goiter, 74, 139
Pulse capillary, 140
Pulse in exophthalmic goiter, 140
Pulsus celer, 140
Pyorrhea alveolaris in pathogenesis of exophthalmic goiter, 89, 173
Pyramidal process of thyroid, 26

Q

Questions involved in etiology of exophthalmic goiter, 82
Quinine and urea injections into thyroid, 296, 385
  hydrobromide in treatment of exophthalmic goiter, 279
    in pregnancy during its administration, 380

R

Race in pathogenesis, 87
Radium in treatment, 307
Rautman, 75, 76, 77, 105
Reading in psychotherapy, 337
Recurrences, postoperative, 343, 344, 384, 391, 394
Reede, E. H., 88
Reflexes in exophthalmic goiter, 171
Regeneration of goiter, postoperative, 343
Reisman, David, 162
Remissions of exophthalmic goiter, postoperative, 343
Renaut's theory in pathogenesis of exophthalmic goiter, 111
Rénon, 110
Resection, subtotal in exophthalmic goiter, 343
Residence and iodine content of thyroid, 42
Respiratory expansion in exophthalmic goiter, 178
Respiratory symptoms in exophthalmic goiter, 178
Rest cure, 245, 247, 329
Rest in psychotherapy, 329
Rest in treatment, 245, 329
Restlessness of patients, 169
Retina in exophthalmic goiter, 163
Reverdin, 93
Rhinitis, chronic, in exophthalmic goiter, 178
Ricaldoni, A., 86
Rice, J. F., 390
Richter, G., 273
Rieder and Verning, 307
Robertson, F. B., 273
Rodagen in treatment, 277
Rogers, J., 275
Rogers and Beebe serum in treatment, 277
Rosenbach's sign, 165
Rosenberg, 86
Rose's goiter heart, 132
Rothacker, 200
Roussy, G., 77, 93, 103, 110, 114, 127
Roussy's theory in pathogenesis, 104
Roux, 238

S

Sahli, H., 138, 140
Sainton, Paul, 153, 191
Sainton and Delherm, 127
Sainton and Fayolle, 162, 176
Sajous, Charles E. de M., 62, 90, 96, 99, 196
Sajous' theory in pathogenesis, 102
Saliva in exophthalmic goiter, 173
Salt bags in treatment, 294
Salvarsan and mercury in treatment, 153
Salzman, S., 61
Sand bags in treatment, 294
Sanford and Blackford, 143
Sanitarium treatment, 226, 227, 247
Savage, 85
Schafer, 33
Schiff, 93
Schinzinger, 179
Schlessinger, 116
Schoenhorn, S., 93
Scleroderma in exophthalmic goiter, 178
Secher, K., 306
Secondary Basedow, 128, 148, 149
  diagnosis of, 149
  differential diagnosis of, 149
  exophthalmic goiter, 128, 148, 149

Secretion of thyroid, 37, 38, 39
  causes of, 37
Seidel, A. and Fenger, F., 41
Selfhood of patients, 315
Senility, tremor in, 166
Serum therapy in treatment, 276
Severity of disease in course and prognosis, 218
Sex and iodine content of thyroid, 42
  and size of thyroid, 25, 29
  in course and prognosis, 215
  in myxedema, 60
  in pathogenesis, 60, 86
  in pathogenesis of goiter, 234
  in thyroid disease, 60
Sexual development and the thyroid, 58
  disturbances, 181
  growth retarded, thyroid extract in, 58
  instinct and balance in psychotherapy, 321
  organs and the thyroid, 58
  relation and thyroid size, 60
  symptoms in exophthalmic goiter, 184
Seymour, H., 300
Shape of goiter, 146
Shape of thyroid gland, 25
Sheehan, Joseph, E., 295
Shell shock and exophthalmic goiter, 195
  as a misnomer, 195
  heart rate in, 135
  in hyperthyroidism, 198
  mental disturbances in, 99
Shock as a factor in cure of exophthalmic goiter (case history), 83
  in pathogenesis, 97
  surgical, in treatment, 395
  thyroid secretion in, 40
Short Rendel, 56
Sielmann, 303
Sign, Dalrymple, 118, 160
  Goffre's, 162
  "hitch," 160
  Jellinek-Teillais, 162
  Kocher's, 161
  Moebius', 118, 160
  Rosenbach's, 165
  Stellwag's, 118
  Suker's, 161
  Von Graefe's, 118, 160
Simonton, T. G., 153
Simple goiter, differential diagnosis of, 147
  in pathogenesis of exophthalmic goiter, 90
  pathogenesis of, 233
Simpson, 303
Sinorzersky, 105
Skin in exophthalmic goiter, 58, 64, 175
  Addisonian melanoderma, 176
  angioneurotic edema, 178
  chloasma, 176
  color, 175
  dermographia, 140, 177
  diminished electrical resistance, 178
  edema, 175
  electrical conductivity, 176
  erythema, 175
  galvanopalpation, 177
  Goetsch test, 178
  hair and nails, 178
  hyperidrosis, 176
  Joffroy's test, 178
  petechiæ, 178
  pigmentation, 64, 176
  pruritis, 177
  scleraderma, 178
  secretion, 175
  scleroderma, 178
  texture, 175
  urticaria, 177
  vasomotor ataxia, 177
  vasomotor instability, 88, 140, 177
  hypothyroidism, 58, 64
Sleep in exophthalmic goiter, 169
Smith, F. D., 197
Smith, J. H., 119
Snow, William B., 309
Social conditions in course and prognosis, 219
Social environments in psychotherapy, 327
Sodium glycerophosphate in treatment, 285
Sodium phosphate in treatment, 285
Sodium salicylate in treatment, 285
Soldiers, exophthalmic goiter in, 195
"Soldiers' irritable heart," 195
Soldiers' phychoses, 196
Spartein treatment, 287
Specifics in treatment, 232
Splanchnic stimulation and adrenal discharge, 65
Spleen and lymphatics, pathology of, 78

Sponge-like nature of hyperplastic thyroid, 74
Spontaneous cure, 392
Stanton, E. McD., 222
Static current in treatment, 309
Statistics erroneous in surgical treatment, 390, 391
Statistics, surgical, 391
Status lymphaticus, postoperative, 343, 395
Stellwag sign, 118, 159
Stengel, Alfred, 84, 113
Stepanoff, 101
Sterility, thyroid extract in, 62
Stern, S., 305
Stiles, P. G., 38
Stokes and Trousseau, 80
Stokes' theory in pathogenesis, 91
Stomach, hemorrhages from, 142
Stoney, F. A., 200, 302
Strophanthus in treatment, 287
Structure of thyroid gland, 27
Strychnine in treatment, 287
Sugar tolerance and ductless gland disease, 120
Sugar tolerance and thyroadrenal function, 65
Suggestion in psychotherapy of exophthalmic goiter, 340
Suicidal tendencies in exophthalmic goiter, 170
Suker's sign of eye, 161
Sulphonal in treatment, 287
Suprarenal disease in thyroid disease, 64
Suprarenal extract in treatment, 64, 274
Suprarenals, pathology of, 77
Surgeons' indecision in treatment, 384, 387
Surgical ''cures,'' 391, 398
  devitalization of patient, 395
  haste in treatment, 395
  indications in treatment, 386
  mortality in treatment, 343, 391, 394
  procedures in treatment, 384
  shock in treatment, 395
  statistics erroneous, 390, 391
  treatment, 343
    analogy of tonsillectomy and thyroidectomy, 383
    cachexia strumipriva in, 384
    choice of operation in, 384
    conservative attitude in, 343
    contraindications to, 21, 343, 344, 381, 395
    criticisms of, 381-400
Surgical ''cures''—Cont'd.
    death from ligation in, 385
    devitalization of patient in, 395
    disappointments in, 343, 344
    fallacy of, 21, 343, 344, 381, 395
    incapable of cure, 343
    indications for, 229, 230, 381
    ligation in, 343, 384
    mishaps in, 343
    mortality rate in, 116, 117, 343, 391, 394
    multiplicity of operations in, 343, 344
    myxedema in, 343, 384, 395
    objections to, 21, 343, 344, 381, 395
    parathyroid removal in, 343, 384
    postoperative, 392
    postoperative exacerbations in, 116, 343, 394
      recurrences in, 343, 344, 384, 391, 394
      tetany in, 384
    regeneration of goiter following, 343
    status lymphaticus in, 343, 395
    subtotal resection in, 343
    sympathectomy in, 105, 343, 385
    tetany in, 343
    thymectomy in, 106, 385
    thyroidectomy in, 343, 384
    vocal paralysis in, 31, 343, 395
Swan, J. M., 153, 179
Sympathectomy in treatment, 343, 385
  in treatment of exophthalmos, 155
Sympathetic (cervical) affection in pathogenesis, 104
  (cervical) autotoxemic irritation of, in pathogenesis, 105
  (cervical) compression and ''false Basedow,'' 90
  (cervical) stimulation of, in cat, 29, 30
  nervous system, stimulation of, 31
    operation in treatment, 105, 343, 385
    theory in pathogenesis, 103
Sympatheticotonia and vagotonia, 119
Sympatheticotonic symptoms, 121
Sympathy psychotherapy, 317
Symptomatic treatment, 232
Symptomatology of acute Graves' disease, 115
Symptoms, abdominal, 174
  circulatory, 130
  cutaneous, 58, 64, 175

Symptoms—Cont'd.
  genitourinary, 181
  intestinal, 175
  nervous, 163
  objective, of heart, 134
  of iodine-Basedow, 130
  of mechanical goiter heart, 132
  of pressure by goiter, 139
  of toxic goiter heart, 132
  respiratory, 178
  sexual, 181
  subjective, of heart, 132
  sympatheticotonic, 121
  urinary, 183
  vagotonic, 120
Syncope from goiter pressure, 139
Syphilis in pathogenesis, 88
  of thyroid, 153
  thyroid swelling in, 88

T

Tachycardia, causes of, 134
  degree of, 133
  diagnosis of, 135, 136
  differential diagnosis of, 135, 136
  in exophthalmic goiter, 117, 134
    constancy of, 134
  of war, 196
  relation to palpitation, 133
Tadpoles, experiments on, with thyroid, 48
Tanzi, 172
Taylor, J. M., 52
Tedeschi and Warburton theory in pathogenesis, 91
Teeth in exophthalmic goiter, 173
Temperament and disposition, 168, 315
  in psychotherapy, 315
Temperature, 178
Tenderness of hyperplastic thyroid, 74, 147
Terror in pathogenesis, 98
Test, diagnostic of exophthalmic goiter, Abderhalden reaction in, 143
  basal metabolism, 208
  blood findings, 210
  complement fixation, 210
  digitalis administration, 210
  Goetsch, 65, 127, 206
  hyperglycemia, 208
  Joffroy's, 178
  pituitary, 207
  thyroid extract administration, 209
Tetanus toxin and thyroid function, 56
Tetany from thyroidectomy, 31
  in mortality of exophthalmic goiter, 214
  postoperative, 343, 384
  thyroid therapy in, 63
Tethelin, 110, 273
  in treatment, 110, 273
Thaon, 109
Theatre in psychotherapy, 338
Theory, adrenal, in pathogenesis, 108
  Basedow, in pathogenesis, 91
  enterotoxemia, in pathogenesis, 94, 96
  Eulenberg and Panas, in pathogenesis, 91
  Friedreich, in pathogenesis, 91
  Gauthier, in pathogenesis, 111
  Gauthier and Moebius, in pathogenesis, 91
  gonad, in pathogenesis, 110
  Graves, in pathogenesis, 91
  hyperthyroidism, in pathogenesis, 111
  Janney, in pathogenesis, 112
  Koeben, in pathogenesis, 104
  Koeben, Aran, Trousseau, and Charcot, in pathogenesis, 91
  Lampé and Klose, in pathogenesis, 112
  Marimon, in pathogenesis, 92
  Marsh, Pral, Maumann and Hensinger, in pathogenesis, 91
  Moebius, criticism of, 112
  Moebius, in pathogenesis, 111
  neurogenic, in pathogenesis, 96
  parathyroid, in pathogenesis, 109
  pituitary, in pathogenesis, 109
  pluriglandular, in pathogenesis, 113
  Renaut, in pathogenesis, 111
  Roussy, in pathogenesis, 104
  Sajous, in pathogenesis. 102
  Stokes, in pathogenesis, 91
  sympathetic, in pathogenesis, 103
  Tedeschi and Warburton, in pathogenesis, 91
  thymus, in pathogenesis, 105
Thompson, G., 95
Thrill of thyroid, 74, 139, 146
Throbbing of goiter, 146
Thymectomy in treatment, 385
Thymic death, thyroid enlargement in, 106
Thymus enlargement, 58, 66, 76, 105, 106
  extract in treatment, 274
  function, 66
  grafting, 106
  hyperplasia, diagnosis of, 66

Thymus enlargement—Cont'd.
    in exophthalmic goiter, 58, 66, 76, 105
  inhibitory action of, on other glands, 106
  pathology of, 76
  regulation of phosphorus by, 67
  relation to thyroid, 65
  removal in treatment, 385
  size, variability of, 66
  theory in pathogenesis, 105
  transplantation with Basedow syndrome, 106
  x-ray therapy of, in treatment, 105, 304
Thyroadrenal function and sugar tolerance, 65
  interrelation, 65
“Thyrodontia,” 53
Thyroid as emotional mentor, 69
  as inhibitor of pancreatic function, 67
  autotransplantation, 38
    conditions for success of, 38, 39
    iodine in, 38
  bruit, 74
  defensive function of, 101
  deficiency, 47, 48
    blood sugar in, 68
  degeneration, 74
  disease and thymus hyperplasia, 65
    blood sugar in, 67
    in relation to size of pituitary, 64
    sex in, 60
    suprarenal disease in, 64
Thyroidectomy and diabetes-mellitus, 68
  and appendectomy, analogy of, 381
  and tonsillectomy, analogy of, 383
  death from, 212, 213, 214
  experimental, pituitary enlargement in, 109
  followed by acute exacerbation, 110
  in aged, 59
  in treatment, 343, 384
  quantity of thyroid removal in, 386
  tetany from, 31
  vocal paralysis following, 31
  with death from acute exacerbation, 116
Thyroid enlargement, bruit in, 32, 74, 139, 147
    in exophthalmic goiter, 91
    in syphilis, 88
    in thymic death, 106
    pulsation in, 32, 74, 139, 147
Thyroid extract and adrenals, 64
    and adrenin content of blood, 64

Thyroid extract—Cont'd.
    and blood pressure, 57, 58
    and circulation, 57
    in chronic rheumatism, 52
    in decayed teeth, 53
    in dermatology, 53
    in eclampsia, 57, 69
    in exophthalmic goiter, 51
    in exophthalmos, 156
    in fractures, 52
    in habitual abortion, 62
    in heart disease, 57
    in hypothyroidism, 53
    in lactation, 61
    in mental aberration, 52
    in myalgia, 52
    in nephritis, 69
    in neuritis, 52
    in pelvic disease, 62
    in retarded sexual growth, 58
    in somnolence, 52
    in sterility, 62
    in syphilis, 56
    in tetany, 63
    in “thyrodontia,” 53, 54
    in treatment of exophthalmic goiter, 270
    in vertigo, 52
    test in diagnosis, 209
  fetal, iodine content of, 41
  gland, accessory, hyperactivity of, 32
    anatomical relations of, 25, 26
    anatomy of, 25
    and circulation, 57
    and female mentality, 59
    and menopause, 61
    and metabolism, 47
    and parathyroids, 63
    and pituitary, 64
    and sexual development, 58
    blood supply of, 28, 29, 30, 31, 36
    capacity of secretion in, 40
    carcinoma of, 151
    development of, 34
    embryology of, 34
    histology of, 27, 28
    in exophthalmic goiter, 143
    iodine content of, 41
    lymphatics of, 29
    malignancy of, 32, 86, 151
    nerve supply of, 29, 30, 37
    physiology of, 36
    pyramidal process of, 26
    structure of, 27, 36
    throbbing of, 32, 74, 138, 147
    tuberculosis of, 153

Thyroid gland—Cont'd.
  - volume of, and circumference of neck, 25
- grafting, 38
- hormone and basal metabolism, 63
  - hyperactivity and the emotions, 40, 69
  - hyperactivity, physiological, 61
- hyperplasia as cause of exophthalmic goiter, 74
- influence on heart, 58
- ingestion and hyperthyroidism, 129
- in pelvic disease, 60, 61
- insufficiency, gastrointestinal tract in, 69
- in treatment of epilepsy, 170
- isthmus, 26

Thyroidin in treatment of exophthalmic goiter, 277

Thyroiditis, 150
- in pathogenesis, 90, 150, 151
- murmur, 32, 74, 139, 147
  - pathology of, 73
- physiology, 36
  - and adrenin therapy, 65
  - and circulation, 57, 130
  - and enterotoxins, 94, 95
  - and gastrointestinal tract, 69
  - and kidneys, 69
  - and liver, 68
  - and metabolism, 47
  - and pancreas, 67
  - and parathyroids, 63
  - and sexual development, 58
  - and skin, 58, 64, 175
  - and suprarenals, 64
  - and thymus, 65
  - antitoxic, 100, 101
  - conclusions on, 71
  - defensive, 181
  - detoxication in, 55
  - diaminization, 62
  - emotional mentor, 69
  - emotions in, 69
  - in diphtheria intoxication, 56
  - in infections, 40
  - ovaries in, 111
  - pituitary in, 64
- pulsation in exophthalmic goiter, 32, 74, 139, 147
- secretion, 37, 38, 39
  - causes of, 37
  - constituents of, 40
  - factors governing, 38
  - in emotions, 40
- shape, 25
- size and sexual relations, 60
  - and virginity, 60

Thyroiditis—Cont'd.
  - in age, 25, 29
  - in children, 25, 29
  - in exophthalmic goiter, 73
  - in females, 25, 29
  - influence of heredity, 25
  - in geographical location, 25
  - in lactation, 60
  - in males, 25, 29
  - in menstruation, 25, 60
  - in parturition, 60
  - in pregnancy, 25, 60, 182
  - in puberty, 60
  - in sex, 25, 29
  - normal standard of, 25
- syphilis of, 153
  - tenderness, 126
  - thrill, 74, 139
  - toxemia as cause of exophthalmic goiter, 83

Thyroidin in treatment of exophthalmic goiter, 277

Thyroiditis, 150
- in pathogenesis, 90, 150, 151

"Thyrotoxicosis" as synonym for exophthalmic goiter, 81

Thyroxin, 43, 49
- and basal metabolism, 45, 49, 50
- functions of, 45
- physiological effects of, 43, 44, 49
- quantity in body, 45
- toxicity of, 44

Tobacco as cause of irritable heart, 201

Tongue, tremor of, 165

Tonsillar disease in pathogenesis, 89

Tonsillectomy and thyroidectomy, analogy of, 383
- in treatment of exophthalmic goiter, 89, 242

Toxemia in pathogenesis, 100

"Toxic goiter" as synonym of exophthalmic goiter, 80

Toxicity of foods, 57

Toxins, intestinal, and the thyroid, 57

Tracheal mobility in thyroid enlargement, 31

Transplantation of goiter tissue, 29, 30, 93, 94
- of hyperplastic thyroid, 29, 30, 93, 94

Traumatism in pathogenesis, 90, 96, 97
- of thyroid in pathogenesis, 90

Treatment of exophthalmic goiter, dietetic, 255
  cream in, 264
  eggs in, 257, 264
  extra nourishments in, 262, 263, 264
  flesh foods in, 265
  meals in, 262
  milk in, 257
Treatment of exophthalmic goiter, electrical, 299
  D'Arsonval current in, 311
  galvanism in, 308
  high frequency current, 310
  Leduc's current, 310
  radium, 307
  static current, 309
  x-ray, 300
  x-ray exposures of thymus, 105
Treatment of exophthalmic goiter, hygienic: 245
  bathing in, 252
  climatotherapy in, 227, 251
  exercise in, 249
  hydrotherapy in, 252
  passive exercise in, 251
  rest cure in, 247
  rest in, 245
Treatment of exophthalmic goiter, general medicinal: 270
  antidiphtheritic serum in, 277
  arsenic in, 281
  atropin in, 286
  belladonna in, 286
  bromides in, 287
  calcium in, 272, 286
  coliform vaccines in, 275
  corpus luteum in, 274
  dechlorination in, 286
  digitalis in, 286
  ergotin in, 288
  erythrol tetranitrate in, 354
  hyoscine in, 287
  ichthyol in, 288
  intestinal antiseptics in, 285
  iodine in, 87, 153, 282, 295
  iron in, 281
  lactic acid ferments in, 275
  lecithin in, 277
  mercury in, 281
  nerve sedatives in, 287
  nonflesh foods in, 265
  nux vomica in, 287
  ovarian extract in, 274
  pancreatic extract in, 275
  parathyroid extract in, 271
  pituitrin in, 64, 110, 272
  quinine hydrobromide in, 279
Treatment Cont'd.
  rodagen in, 277
  Rogers and Beebe serum in, 277
  salvarsan in, 281
  sodium glycerophosphate in, 285
  sodium phosphate in, 285
  sodium salicylate in, 285
  spartein in, 287
  strophanthus in, 287
  strychnine in, 287
  sulphonal in, 287
  suprarenal extract in, 274
  tethelin in, 273
  thymus extract in, 274
  thyroid extract in, 270
  thyroidin in, 277
  trional in, 287
  veronal in, 261, 262, 287
Treatment of exophthalmic goiter, local: 291
  adhesive plaster in, 294
  boiling water injections in, 297, 385
  carbolic acid injections in, 295
  collodion in, 294
  ice bags in, 252, 294
  iodine application in, 292
  iodine injections in, 92, 295
  Leiter coils in, 252, 253
  oil injections in, 285
  prescriptions in, 293
  quinine and urea injections into thyroid, 295, 296, 385
  salt bags in, 294
  sand bags in, 294
  tonsillectomy in, 89
  venesection in, 287
Treatment of exophthalmic goiter, miscellaneous considerations:
  appetite in, 260
  average case, prescriptions in, 288
  colectomy in, 385
  conclusions on, 381
  contraindications to operation in, 395
  cooperation in, 231
  diet lists in, 266
  digestive disturbances in, 260
  duration of, 211, 225, 231
  duration of, in course and prognosis, 225
  early diagnosis in, 230
  gain of weight in, 258, 259, 269
  gastrointestinal hygiene in, 254
  gynecology in, 111, 183
  home in, 227, 247
  hospital in, 226, 227, 247

Treatment—Cont'd.
  index of improvement in, 258, 259, 269
  individualization in, 231, 270, 380
  internists' opinions on, 396
  ligation in, 343, 384
  number of meals in, 262
  objections to surgery in, 394
  operations in, 384
  opinions of internists on, 396
  opinions of surgeons on, 387
  organotherapy in, 270
  postoperative exacerbations in, 116, 343, 394
  postoperative recurrences of, 343, 344, 384, 391, 394
  sanitarium in, 226, 227, 247
  serum therapy in, 276
  specifics in, 232
  surgery in, 200, 229, 381, 384
  surgical indications in, 229
  surgical, result of, 223
  sympathetic operation in, 105
  symptomatic, 232
  weight in, 258, 259, 269
Treatment of exophthalmic goiter, psychotherapy: 311
  confession, 319
  conversation, 338
  correction of social environments, 327
  esthetic recreation, 339
  exercise, 249
  individualization, 320
  laughter, 330
  lectures, 338
  mental equanimity, 339
  mental suggestion, 340
  music, 334
  reading, 337
  rest, 329
  sympathy and affection, 317
Treatment of exophthalmos, sympathectomy in, 155
Treatment of goiter by colectomy, 237
  by x-rays, 241
  intestinal antiseptics in, 236
  tonsillectomy in, 242
  vaccines in, 237
Treatment of secondary Basedow, 148
  of syphilitic thyroid, 153
  of vagotonia, adrenalin in, 120
Trembling in exophthalmic goiter, 164
Tremor, calcium therapy in, 63
  constant, 165
  differential diagnosis of, 165, 166, 167
  hereditary, 167
  in chorea, 167
  in emotional excitement, 165
  in exophthalmic goiter, 118, 163
  in intoxications, 165
  in neurasthenia, 166
  in paralysis agitans, 166
  in senility, 166
  "intention," 165
  occurrence of, 164, 165
  of body, 167
  of eye balls, 161, 165
  of hysteria, 166
  of multiple sclerosis, 167
  of organic nervous disease, 166
  of tongue, 165
  parathyroid therapy in, 63
  passive, 165
  varieties of, 165
Trional in treatment, 287
Trousseau, 77, 103, 155
Tuberculosis and exophthalmic goiter, 88, 153, 179, 180
  differentiated from exophthalmic goiter, 180, 188
  erroneous diagnosis of, in exophthalmic goiter, 117
  in course and prognosis, 218
  in mortality of exophthalmic goiter, 213
  in pathogenesis, 88
  of thyroid, 153

U

Ulceration of cornea, 161
Urinary findings, 183, 184
Urticaria, 177

V

Vaccines, coliform, in treatment, 275
  in treatment of goiter, 237
Vagotonia and sympatheticotonia, 119
  ductless glands in, 120
  parasympathetic stimulation in, 121
  treatment with adrenalin, 120
Vagotonic symptoms, 120
Vagus irritation, anaphylaxis in, 120
Vas, 101
Vascularity of thyroid as cause of secretion, 37, 38
Vascular throbbing, 74, 139
Vasoconstricting influence of pituitary on thyroid, 109

Vasomotor ataxia, 177
  instability, 88, 140, 177
    in hyperthyroidism, 58, 88, 140, 177
Veil, H. H., 62
Venesection in treatment, 287
Verdun, 34
Veronal in treatment, 261, 262, 287
Vertigo from goiter pressure, 32, 139
Vetlesen, 285
Vibration of body, 74
Vigouroux, 176
Vinay, 110
Virginity, thyroid size in, 60
Vision in exophthalmic goiter, 163
Vocal paralysis, postoperative, 31, 343, 395
Voice alteration from goiter pressure, 139, 179
Vomiting, 174
Von Basedow, 80
Von Cyon, 57
Von Fellenburg, 62
Von Graefe sign, 118, 160
Von Pezhold, 153

W

Walter, 302
War conditions in pathogenesis, 197
"War tachycardia," 196
Wasting of body, 119
Water, boiling, injections into thyroid, 297
Water in pathogenesis, 234
Watson, L. F., 296
Weber, L., 281
Weight of body, 255, 258, 259, 269
Welsh, 33
West, 176
White, H., 396
White and Aub, 138
Wiesel, 77
Williams, L., 243
Wilson, L. B., 75, 103
Wilson, Poynton and Stoney, 199
Work in psychotherapy, 329
Wright, Sir Almroth E., 101

X

X-ray in treatment, 300
  dangers of, 306, 307
X-ray treatment of goiter, 241
X-ray therapy of thymus in treatment, 105, 304

Z

Zentmayer, Wm., 161

LANE MEDICAL LIBRARY

To avoid fine, this book should be returned on
or before the date last stamped below.

OCT 31 1921
MAR -2 1934
FEB 17 1922
JAN -2 '23
RETURN TO Branch
Jan 2 '24
NOV -4 '24
FEB 10 1928
OCT 12 28
JUL -8 '29
MAR 21 1932
AUG 30 1932
DEC 11 1933

L656 Fram, I. 51142
F81 Exophthalmic goiter.
1920

NAME	DATE DUE
R. L. A. Sh	OCT 31 1921 FEB 17 1922
Fresno Co. Library	JAN -2 23
J Marion Read.	NOV -4
William S. Cam	[illegible]
H Shimer	OCT 11
[illegible]	
	JUL -8 '29
H O Barker.	MAR 21 1932
Delos Kent.	AUG 30 193
G B Schunke	NOV 12
R R Hartman	1934